Table 18: **gp160**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(2–10)	gp160(2–10 IIIB)	RVKEKYQHL	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0801 epitope				
gp160(2–10)	gp160(2–10 IIIB)	RVKEKYQHL	HIV-1 infection	human(B8)	[Sipsas (1997)]
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • Type-specific epitope, unique to the LAI and IIIB because of a deletion of three amino acids that are present in all other subtype B HIV-1s • RVKGIRKNYQHL, a variant found in JRCSF, was not recognized • This epitope is in the signal sequence of gp120				
gp160(2–10)	gp120(2–10)	RVKEKYQHL	HIV-1 infection	human(B8)	[Day (2001)]
	• B8-restricted CTL that accounted for about 1/3 of the total CTL response in one individual				
gp160(6–15)	gp120(6–15 CM243 CRF01)	TQMNWPNLWK	HIV-1 exposed seronegative	human(A11)	[Sriwanthana (2001)]
	• Epitope name: E6-15. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11				
gp160(6–15)	gp120(6–15 CM243 CRF01)	TQMNWPNLWK	HIV-1 infection	human(A11)	[Bond (2001)]
	• HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it • This epitope was not conserved in other subtypes, and exact matches were rare				
gp160(29–49)	gp120( )	AAEQLWVTVYYGVPV-WKEAT	HIV-1 infection	human(A11)	[Weekes (1999b)]
	• Peptide 7035.1: Almost all CD8+ T-cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied				

- The clonal composition of TCR Vβ responses was studied and was found to be highly focused, with one TCR β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ6

gp160(31–39)	gp120(30–38)	AENLWVTVY	HIV-1 infection	human(B44)	[Day (2001)]
gp160(31–39)	gp120(30–38 SF2)	AENLWVTVY	HIV-1 infection	human(B44)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B44+ individuals that had a CTL response to this epitope broken down by group: 1/8 group 1, 2/3 group 2, and 3/4 group 3

gp160(31–40)	gp160(30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human(B*4402)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*4402 epitope

gp160(31–40)	gp160(30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human(B44)	[Borrow (1997), Borrow & Shaw(1998), Goulder (1997a)]

- Two CTL lines from the patient WEAU were studied – one had an optimal peptide of (A)AENLWVTVYY, and the other (A)AENLWVTVY, and both responded equally well with one or two N-term Alanines
- Rapidly post-infection, a strong immunodominant response was observed against this epitope
- The naturally occurring forms of the peptide found in WEAU were tested as targets for early WEAU CTLs – the form TENLWVTVY was as reactive as the wild type AENLWVTVY – but the forms AKNLWVTVY, AGNLWVTVY, AANLWVTVY did not serve as targets
- The glutamic acid in the second position is a B44 anchor residue
- [Goulder (1997a)] and [Borrow & Shaw(1998)] are reviews of immune escape that summarizes this study in the context of CTL escape to fixation

gp160(31–55)	gp120(32–56 LAI)	TEKLWVTVYYGVPVW-KEATTTLFCA	Vaccine	human(B18)	[Johnson (1994a)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees

gp160(31–55)	gp120(32–56 LAI)	TEKLWVTVYYGVPVW-KEATTTLFCA	Vaccine	human(B18)	[Ferris (1999), Hammond (1995)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- This peptide can be processed for HLA-B18 presentation by both TAP-1/2 independent and dependent pathways

gp160(33–42)	gp120(32–41 LAI)	KLWVTVYYGV	Vaccine	human(A2)	[Dupuis (1995)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- CTL from HLA-A2 positive subject react with this peptide

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gp160(33–42)	Env(32–41 clade B)	KLWVTVYYGV	HIV-1 infection, Vaccine	human(A2.1)	[Kundu (1998a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses

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gp160(34–55)	gp120(25–46 BRU)	LWVTVYYGVPVWKEA-TTTLFCA	HIV-1 infection	human(A2)	[Dadaglio (1991)]

- Defined through peptide blocking of CTL activity, and Env deletions

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gp160(36–46)	gp120(36–46 CM243 CRF01)	VTVYYGVPVWR	HIV-1 exposed seronegative	human(A11)	[Sriwanthana (2001)]

- Epitope name: E36-4. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11

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gp160(36–46)	gp120(36–46 CM243 CRF01)	VTVYYGVPVWR	HIV-1 infection	human(A11)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined
- 1/8 tested FSWs recognized this epitope
- This epitope was only conserved in CRF01 and subtypes B and C, and exact matches were uncommon

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gp160(36–46)	gp120( )	VTVYYGVPVWK	HIV-1 infection	human(A11 and A*6801)	[Threlkeld (1997)]

- Study of the fine specificity of an A3-like-HLA-super-type epitope (the A3-super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801)
- The A3 super-type is characterized as a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position
- While most lines were specific, a promiscuous cloned CTL line was derived from an HIV+ donor that could recognize this epitope presented by either A11 or A*6801

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gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	Vaccine	human(A*0301)	[Johnson (1994b)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- Multiple CTL clones obtained from two vaccinees
- C. Brander notes that this is an A*0301 epitope in the 1999 database

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gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	Vaccine	human(A*0301)	[Brander & Goulder(2001)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- C. Brander notes this is an A*0301 epitope

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gp160(37–46)	Env( )	TVYYGVPVWK	Vaccine	SJL/J HLA trans-genic mice(A11)	[Ishioka (1999)]

Vaccine: *Vector/type:* DNA *HIV component:* polyepitope

- A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed
- The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans
- HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong

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gp160(37–46)	gp120(37–46)	TVYYGVPVWK	Vaccine	human(A3)	[Carruth (1999)]

Vaccine: *Vector/type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease

- The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease)
- CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination
- CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls
- The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen

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gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	HIV-1 infection	human(A3)	[Goulder (1997e), Goulder (1997a)]

- Identical twin hemophiliac brothers were both infected with the same batch of factor VIII
- One had a response to this epitope, the other did not
- [Goulder (1997a)] is a review of immune escape that summarizes this study

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gp160(37–46)	gp120(36–45)	TVYYGVPVWK	HIV-1 infection	human(A3)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

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gp160(37–46)	gp120(37–46)	TVYYGVPVWK	HIV-1 infection	human(A3)	[Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant

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gp160(37–46)	Env(49–58)	TVYYGVPVWK	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

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gp160(37–46)	gp120(38–41 LAI)	TVYYGVPVWK	Vaccine	human(A3.1)	[Johnson (1994a)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- Highly conserved epitope recognized by multiple CTL clones from vaccinee

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gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	Vaccine	human(A3.1)	[Ferris (1999), Hammond (1995)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- This peptide can be processed for HLA-A3.1 presentation by TAP-1/2 independent and dependent pathways

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gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	HIV-1 infection	human(B*0301)	[Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found

- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and was appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

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gp160(38–48) gp120(45–55) VYYGVPVWKEA HIV-1 infection human(Cw7) [Nehete (1998)]

- Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one
- HLA-C antigens are expressed on lymphoid cells to a lesser extent than either HLA-A or -B
- HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T-cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing

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gp160(42–51) gp120(42–51 PV22) VPVWKEATTT HIV-1 infection human(B*5501) [Brander & Goulder(2001)]

- C. Brander notes this is a B*5501 epitope

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gp160(42–51) gp120(42–51 PV22) VPVWKEATTT HIV-1 infection human(B55) [Brander & Walker(1995)]

- P. Johnson, unpublished

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gp160(42–51) gp120(41–55) VPVWKEATTT HIV-1 infection human(B55) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

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gp160(42–52) gp120(42–52) VPVWKEATTTL HIV-1 infection human(B*3501) [Brander & Goulder(2001)]

- C. Brander notes this is a B*3501 epitope

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gp160(42–52) gp120(42–52 PV22) VPVWKEATTTL HIV-1 infection human(B35) [Cao (1997)]

- VPVWKEATTTL is the consensus sequence for clades B and D
- VPVWKDAETTL is the consensus sequence for clade A and it is cross-reactive
- VPVWKEADTTL is the consensus sequence for clade C and it is cross-reactive
- VPVWKEADTTL is the consensus sequence for clade E and even with three substitutions still retains some cross-reactivity

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gp160(42–52) gp120(41–51) VPVWKEATTTL HIV-1 infection human(B35) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

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gp160(42–61)	gp120(49–68)	VPVWKEATTTLFCAS-DAKAY	*in vitro* simulation	human( )	[Lieberman (1995)]

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide

gp160(42–61)	gp120(49–68 SF2)	VPVWKEATTTLFCAS-DAKAY	HIV-1 infection	human( )	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- Three of these 11 had CTL response to this peptide
- The responding subjects were HLA-A2, A3, B8, B62; HLA-A3, A24, B7, B38

gp160(42–61)	gp120(49–68 SF2)	VPVWKEATTTLFCAS-DAKAY	HIV-1 infection	human( )	[Lieberman (1997b)]

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients

gp160(50–59)	Env(62–71)	TTLFCASDAK	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

gp160(51–59)	Env(63–71)	TLFCASDAK	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

gp160(52–61)	gp120(59–68 HXB2)	LFCASDAKAY	HIV-1 infection	human(A*2402)	[Lieberman (1992)]

- CTL epitope defined by T-cell line and peptide mapping
- C. Brander notes that this is an A*2402 epitope in the 1999 database

gp160(52–61)	gp120(53–62 LAI)	LFCASDAKAY	HIV-1 infection	human(A*2402)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*2402 epitope

gp160(52–61)	gp120(53–62)	LFCASDAKAY	HIV-1 exposed seronegative, HIV-1 infection	human(A24)	[Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

gp160(52–61)	gp120(53–62 LAI)	LFCASCAKAY	HIV-1 infection	human(B38)	[Shankar (1996)]
• Uncertain whether optimal, binds A24 as well					
gp160(52–71)	gp120(59–78)	LFCASDAKAYDTEVHI-NVWAT	*in vitro* simulation	human( )	[Lieberman (1995)]
• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide					
gp160(52–71)	gp120(59–78 SF2)	LFCASDAKAYDTEVHI-NVWAT	HIV-1 infection	human( )	[Lieberman (1997a)]
• Of 25 patients, most had CTL specific for more than one HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2 and B-21					
gp160(62–80)	gp120(69–88 SF2)	DTEVHNVWATHACVP-TDPN	HIV-1 infection	human( )	[Lieberman (1997a)]
• Of 25 patients, most had CTL specific for more than one HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2 and B-21					
gp160(78–86)	Env(77–85)	DPNPQEVVL	HIV-1 infection	human(A*3501)	[Ogg (1999)]
• CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVANTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient • Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days					
gp160(78–86)	gp120(77–85)	DPNPQEVVL	HIV-1 infection	human(B*3501)	[Ogg (1998b)]
• This epitope was included to illustrate the specificity of HIV-tetrameric staining, in a cross-sectional study correlating HLA A*0201 CTL effector cells and low viral load					
gp160(78–86)	gp120(77–85 SF2)	DPNPQEVVL	HIV-1 infection	human(B*3501)	[Brander & Goulder(2001)]
• C. Brander notes this is a B*3501 epitope					
gp160(78–86)	gp120(77–85 SF2)	DPNPQEVVL	HIV-1 infection	human(B*3501)	[Tomiyama (1997)]
• A CTL clone responsive to this epitope was obtained • 2/7 B35-positive individuals have a CTL response to this epitope					

- This epitope is highly variable
- The substitutions: 1N, 3S and 7I, 7L and 9M, 8I, 8K all abrogate specific CTL lysis, but of these only 8K reduces binding to B*3501
- The substitution 8V to 8E does not reduce specific CTL activity

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gp160(78–86) Env(77–85) DPNPQEVVL HIV-1 infection human(B35) [Dyer (1999)]

- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load

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gp160(78–86) ( ) DPNPQEVVL HIV-1 infection human(B35) [Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and was appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

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gp160(78–86) ( ) DPNPQEVVL HIV-1 infection human(B35) [Kawana (1999)]

- HLA B35 is associated with rapid disease progression
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation

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gp160(78–86) gp120(77–85 SF2) DPNPQEVVL HIV-1 infection human(B35) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3

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gp160(78–86)	gp120(77–85 SF2)	DPNPQEVVL	HIV-1 infection	human(B35, B51)	[Shiga (1996)]
• Binds HLA-B*3501 and B*5101 – CTL can kill gp120-vaccinia virus-infected cells carrying B35 or B51					
gp160(78–86)	gp120(77–85)	DPNPQEVVL	HIV-1 exposed seronegative, HIV-1 infection	human(B51)	[Kaul (2001a)]
• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers					
gp160(103–111)	Env(102–110)	QMHEDIISL	HIV-1 infection	human(A*0201)	[Kmieciak (1998a)]
• Epitope name: 4.3. CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues; • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*; • Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity; • Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vβ repertoire;					
gp160(104–119)	gp120(111–126 IIIB)	MQEDIISLWDQSLKPC	*in vitro* stimulation	human( )	[Macatonia (1991)]
• Primary CTL response with cells from non-infected donors stimulated by the peptide					
gp160(105–117)	gp120( )	HEDIISLWDQSLK	HIV-1 infection	chimpanzee( )	[Lubeck (1997)]
• No epitope-specific CTL were detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant despite a response to peptides P18 and T1 • Helper and cytotoxic T-cells have been found to be stimulated by this peptide (T2)					
gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 exposed seronegative	human( )	[Pinto (1995)]
• CTL and T helper cell reactivity in healthcare workers exposed to HIV					
gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human(A2)	[Clerici (1991)]
• Epitope name: T2. Helper and cytotoxic T-cells can be stimulated by this peptide (T2)					
gp160(108–116)	Env(107–115 clade B)	IISLWDQSL	Vaccine	human(A2.1)	[Kundu (1998a)]
Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses					

gp160(109–117)	Env(109–117 CM243 CRF01)	ISLWDQSLK	HIV-1 exposed seronegative	human(A11)	[Bond (2001)]

- Epitope name: E109-117. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11, and had been predicted to be a possible A11 epitope using Epimer in [Bond (2001)]

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gp160(112–130)	gp120(119–139 SF2)	WDQSLKPCVKLTPLC-VSLK	HIV-1 infection	human( )	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- One of these 11 had CTL response to this peptide
- The responding subject was HLA-A2 and B-21

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gp160(117–126)	Env(72–81)	KPCVKLTPLC	HIV-1 infection	human(B7)	[Jin (2000b)]

- This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor
- A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing

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gp160(121–129)	Env(120–128)	KLTPLCVTL	HIV-1 infection	human(A*0201)	[Kmieciak (1998a)]

- Epitope name: D1. CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues;
- The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*;
- Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity;
- Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vβ repertoire;
- In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher over time;

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gp160(121–129)	Env( )	KLTPLCVTL	HIV-1 infection	human(A2-supertype, A*0201)	[Altfeld (2001d)]

- Epitope name: Env-134. HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acutely infected individuals recognized at least 1 (median of 1 and maximum of 2)

- 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT
- 0/12 acutely infected individuals recognized this epitope
- KLTPLCVTL binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0203 and A*6802 (highest affinity)

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gp160(121–129) gp120(120–128 LAI) KLTPLCVTL Vaccine human(A2) [Dupuis (1995)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- CTL from HLA-A2 positive subject react with this peptide

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gp160(121–129) gp120(120–128) KLTPLCVTL Vaccine human(A2) [Woodberry (1999)]

Vaccine: *Vector/type:* vaccinia *HIV component:* polyepitope

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested
- KLTPLCVTL was recognized by 3 of the patients

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gp160(121–129) gp120(120–128) KLTPLCVTL HIV-1 infection human(A2) [Kundu (1998b)]

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated
- KLTPLCVTL is a conserved HLA-A2 epitope included in this study – all six patients had this sequence as their HIV direct sequence, and a detectable CTL response
- CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine

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gp160(121–129) gp120(120–128) KLTPLCVTL HIV-1 infection human(A2) [Kmieciak (1998b)]

- Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product

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gp160(121–129) gp120(121–129) KLTPLCVSL *in vitro* stimulation human(A2) [Zarling (1999)]

- This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses

- Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA
- A weak response to KLTPLCVSL was stimulated using macrophages as the APC
- No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL

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gp160(121–129) gp120(120–128) KTLPLCVTL HIV-1 infection human(A2) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

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gp160(121–129) Env(134–142) KLTPLCVTL HIV-1 infection human(A2 supertype) [Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)

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gp160(121–129) Env( ) KLTPLCVTL Vaccine SJL/J HLA transgenic mice(A2.1) [Ishioka (1999)]

Vaccine: *Vector/type:* DNA *HIV component:* polyepitope

- A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed
- The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans
- HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection

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gp160(121–129) Env(120–128 clade B) KLTPLCVTL Vaccine human(A2.1) [Kundu (1998a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses

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gp160(156–165)	gp120(156–165)	NCSFNISTSI	HIV-1 infection	human(Cw*08)	[Ferris (1999)]

- Recognized by CTL clone LWF A5, isolated from a lab worker exposed to HIV-1 in 1985
- The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains two N-linked glycosylation sites that are glycosylated in Env
- Only peptide that has been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) was recognized: the aspartic acid at position 5 was critical, position 1 could be either D or N
- This peptide also contains a Cys involved in a disulfide linkage but reducing conditions did not effect recognition by CTL clone LWF A5
- The HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules
- The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively

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gp160(156–165)	gp120(156–165 IIIB)	NCSFNISTSI	HIV-1 infection	human(Cw8)	[Sipsas (1997)]

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB
- NCSFNITTSI, a variant found in HIV-1 MN, was not recognized, thus this epitope was type-specific
- NCSFNISTSI contains two potential N-linked glycosylation sites and cysteine residue, possibly related to the requirement for a high sensitizing dose of peptide for CTL activity

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gp160(188–207)	gp120(193–212 BRU)	TTSYTLTSCNTSVITQA-CPK	HIV-1 infection	human(A2)	[Dadaglio (1991)]

- Defined through blocking CTL activity, and Env deletions

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gp160(191–200)	gp120(194–202 CM243 CRF01)	YRLINCNTSV	HIV-1 infection	human(A2)	[Sriwanthana (2001)]

- Epitope name: E191-200. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2

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gp160(191–200)	gp120(194–202 CM243 CRF01)	YRLINCNTSV	HIV-1 infection	human(A2)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by four amino acids, KLTSCNTSV
- This epitope was somewhat conserved in 4/8 subtypes: CRF01 (E), B, C, and D

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gp160(192–200)	gp120(192–199)	KLTSCNTSV	HIV-1 infection	human(A*02)	[Rinaldo (2000)]

- Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection

gp160(192–200)	gp120(192–199 HXB2R)	KLTSCNTSV	HIV-1 infection	human(A2)	[Brander (1995)]

- Epitope predicted on HLA binding motif, and studied in the context of inclusion in a synthetic vaccine

gp160(192–200)	gp120(192–199)	KLTSCNTSV	HIV-1 infection	human(A2)	[Huang (2000)]

- The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed
- Increases in γ interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-γ-production ELISPOT

gp160(192–200)	gp120(197–205)	TLTSCNTSV	Peptide-HLA interaction	human(A2)	[Garboczi (1992)]

- Crystallization of HLA-A2 molecules complexed with antigenic peptides – refers to Dadaglio *et al* 1991

gp160(192–200)	gp120(199–207)	TLTSCNTSV	HIV-1 infection	human(A2.1)	[Brander (1996)]

- This epitope was recognized by PBMC from 6/14 HIV+ asymptomatic patients
- This epitope was used along with pol CTL epitope ALQDSGLEV and a tetanus toxin T helper epitope for a synthetic vaccine
- This vaccine failed to induce a CTL response, although a helper response was evident

gp160(192–211)	gp120(199–219 SF2)	SLTSCNTSVITQACPK-VSFE	HIV-1 infection	human( )	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- One of these 11 had CTL response to this peptide
- The responding subject was HLA-A2, -B21

gp160(201–225)	gp120(201–225 LAI)	ITQACPKVSFEPIPHYC-APAGFAI	Vaccine	human(CD4+ CTL)	[Johnson (1994b), Johnson (1994a)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- CD4+ CTL isolated from LAI IIIB gp160 vaccinees

gp160(202–221)	gp120(209–228)	TQACPKVSFEPIPIHYC-APA	*in vitro* stimulation	human( )	[Lieberman (1995)]

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide

gp160(202–221)	gp120( )	TQACPKVSFEPIPIHYC-APA	HIV-1 infection	human( )	[Weekes (1999b)]

- Almost all CD8+ T-cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population
- HIV CTL responses to 3 Env and 2 Gag peptides were studied
- The clonal composition of TCR Vβ responses were studied and was found to be highly focused, with one TCR β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.1

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gp160(202–221)	gp120( )	TQACPKVSFEPIPIHYC-APA	HIV-1 infection	human( )	[Weekes (1999a)]

- Epitope name: Peptide 740.18. Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28-CD8+ CTLp populations

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gp160(202–221)	gp120(209–228 SF2)	TQACPKVSFEPIPIHYC-APA	HIV-1 infection	human( )	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- One of these 11 had CTL response to this peptide

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gp160(202–221)	gp120(209–228 SF2)	TQACPKVSFEPIPIHYC-APA	HIV-1 infection	human( )	[Lieberman (1997b)]

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients

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gp160(207–216)	gp120( )	KMTFEPIPIH	HIV-1 infection	human(A29)	[Cao (2000)]

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent-specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype
- CTL derived from subtype A clade infection (patient SP 528), recognized the subtype A version of the peptide (KMSFEPIPIH), had a slightly reduced specific lysis using the B clade version of the peptide (KVSFEPIPIH), and no lysis using the D clade version of the epitope (KVTFEPIPIH)
- Patient SP 528 is HLA A1, A29, B57, B81, Bw4, Bw6

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gp160(208–217)	gp120( )	VSFEPIPIHY	HIV-1 exposed seronegative	human(A29)	[Kaul (2000)]

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-IFN responses in the cervix – systemic CD8+ T-cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T-cell responses
- Low risk individuals did not have such CD8+ cells

- CD8+ T-cell epitopes DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women

gp160(208–217)	gp120(263–272)	VSFEPIPHY	HIV-1 exposed seronegative, HIV-1 infection	human(A29)	[Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

gp160(209–217)	( )	SFEPIPIHY		(A29)	[Altfeld(2000), Brander & Goulder(2001)]

gp160(209–217)	gp120(213–221 SF2)	SFEPIPIHY	HIV-1 infection	human(A29)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-A29+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/0 group 2, and 0/0 group 3

gp160(212–231)	gp120( )	PIPIHYCAPAGFAILKC-NNK	HIV-1 infection	human( )	[Weekes (1999a)]

- Epitope name: Peptide 740.19. Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28-CD8+ CTLp populations

gp160(212–231)	gp120(219–238 HXB2)	PIPIHYCAPAGFAILKC-NNK	HIV-1 infection	human( )	[Lieberman (1992)]

- CTL epitope defined by T-cell line and peptide mapping

gp160(212–231)	gp120(219–238)	PIPIHYCAPAGFAILKC-NNK	*in vitro* stimulation	human( )	[Lieberman (1995)]

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide

gp160(212–231)	gp120( )	PIPIHYCAPAGFAILKC-NNK	HIV-1 infection	human(A2)	[Weekes (1999b)]

- Almost all CD8+ T-cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population
- HIV CTL responses to 3 Env and 2 Gag peptides were studied

- The clonal composition of TCR Vβ responses was studied and was found to be highly focused, with one TCR β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.6

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gp160(212–231) gp120( ) PIPIHYCAPAGFAILKC-NNK HIV-1 infection human(B57) [Jin (1998b)]

- Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction
- Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK

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gp160(237–246) Env( ) GPCKNVSTVQ human(B56) [De Groot (2001)]

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay
- GPCKNVSTVQ was newly-defined as an epitope in this study, was shown to stimulate an ELISPOT response, and to bind to HLA-B7

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gp160(239–247) gp120(241–249 LAI) CTNVSTVQC HIV-1 infection human(Cw8) [Sipsas (1997)]

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB
- CTNVSTVQC contains a potential N-linked glycosylation site and cysteine residues, possibly related to a requirement for a high sensitizing dose of peptide for CTL activity

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gp160(242–261) gp120(249–268) VSTVQCTHGIRPVVST-QLLL *in vitro* stimulation human( ) [Lieberman (1995)]

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide

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gp160(242–261) gp120(249–268 SF2) VSTVQCTHGIRPVVST-QLLL HIV-1 infection human( ) [Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- One of these 11 had CTL response to this peptide
- The responding subject was HLA-2, -B21

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gp160(242–261) gp120(249–268) VSTVQCTHGIRPVVST-QLLL HIV-1 infection human( ) [Lieberman (1997b)]

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients

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gp160(252–260) gp120(255–263 SF2) RPIVSTQLL HIV-1 infection human(B*3501) [Tomiyama (1997)]

- A CTL clone responsive to this epitope was obtained

- Only 1/7 B35-positive individuals had a CTL response to this epitope
- An I to V substitution at position 3 reduces specific lysis, but not binding to B*3501
- A Q to H substitution at position 7 abrogates specific lysis, but not binding to B*3501

gp160(252–260)	gp120(255–263 SF2)	RPIVSTQLL	HIV-1 infection	human(B35)	[Shiga (1996)]

- Binds HLA-B*3501

gp160(252–260)	( )	RPIVSTQLL	HIV-1 infection	human(B35)	[Kawana (1999)]

- HLA B35 is associated with rapid disease progression
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation

gp160(252–261)	Env( )	RPVVSTQLLL		human(B7)	[De Groot (2001)]

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay
- RPVVSTQLLL was one of the 15, and had been previously identified as an HLA-B7 epitope, and was confirmed in this study

gp160(252–271)	gp120(256–275 LAI)	RPVVSTQLLLNGSLAE-EEVV	HIV-1 infection	human(B7)	[Shankar (1996)]
gp160(291–307)	gp120(295–312 BRU)	SVEINCTRPNNNTRKSI	HIV-1 infection	human(A2)	[Dadaglio (1991)]

- Defined through blocking CTL activity, and Env deletions

gp160(297–322)	gp120(297–322 IIIB)	TRPNNNTRKRIRIQRG-PGRAFVTIGK	Vaccine	murine(H-2D^d)	[Chang (1999)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3 *Stimulatory Agents:* liposome

- Induction of peptide-specific CTLs in BALB/c mice was dependent on immunization with peptide encapsulated liposomes containing MPL as adjuvant
- T26K (26mer) elicited a stronger AB and CTL response than R15K (a V3 15mer, RIQRGPGRAFVTIGK)

gp160(297–330)	Env(303–335 BX08)	TRPNNNTRKSIHIGPG-RAFYATGEIIGDIRQAH	Vaccine	human( )	[Gahery-Segard (2000)]

Vaccine: *Vector/type:* lipopeptide *HIV component:* six peptides

- Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial

- A CD4+ T-cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide
- 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees
- None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed

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gp160(298–307)	gp120(298–307)	RPNNNTRKSI	HIV-1 infection	human(B*07)	[Ferris (1999), Hammond (1995)]

- The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains an N-linked glycosylation site that is glycosylated in Env
- Peptide that had been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) (RPNDNTRKSI) was recognized a 100-fold more efficiently than either glycosylated or non-glycosylated RPNNNTRKSI
- Position 5 is not involved with HLA B*07 binding, so is probably important for TCR recognition
- HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules
- The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively

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gp160(298–307)	gp120(302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*0702 epitope

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gp160(298–307)	gp120(302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human(B7)	[Safrit (1994b)]

- CTL from two acute seroconversion cases

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gp160(298–307)	gp120(302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human(B7)	[Hammond (1995)]

- Peptide processed by a TAP-1/2-dependent pathway only
- CTL from an acute seroconverter

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gp160(298–307)	gp120(302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human(B7)	[Wolinsky (1996)]

- Longitudinal study of epitope variation *in vivo*

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gp160(298–307)	gp120(302–311 clade B)	RPNNNTRKSI	HIV-1 infection	human(B7)	[Wilson (1998b)]

- The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed

- Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope RPNNNTRKSI is immunodominant, conserved between the LAI and clade A and C strains, but is very divergent in MN (RPNYNKRKRI), and that this epitope might be dominating the specificity of the response in the HLA B7 individuals

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gp160(298–307) gp120(303–312 SF2) RPNNNTRKSI HIV-1 infection human(B7) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 1/3 group 2, and 1/1 group 3

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gp160(298–307) gp120(298–307) RPNNNTRKSI HIV-1 infection human(B7) [Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope

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gp160(298–307) gp120(303–312 IIIB) RPNNNTRKSI HIV-1 infection human(B7?) [Wilson (1996)]

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study
- RPNNNTRKDI and RPNNNTRKGI, naturally occurring variants, were found in non-transmitting mother – ability to recognize these variants was not determined

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gp160(303–322) gp120( ) TRKSIHIGPGRAFYTT-GE Vaccine murine BALB/c( ) [Luo (1998)]

Vaccine: *Vector/type:* virus-like particle *Strain:* B subtype consensus *HIV component:* gag, V3

- Intramuscular injection of chimeric gag-env virus-like particles (VLPs) containing V3 loop sequences into BALB/c mice induce V3 specific CTL – TRKSIHIGPGRAFYTTGE is a B subtype consensus that stimulated a cross-reactive CTL response

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gp160(304–318) gp120(304–318 IIIB) RKSIRIQRGPGRAFV Vaccine murine(H-2^d) [Kang (1999)]

Vaccine: *Vector/type:* virus-like particle *Strain:* HIV-2 VLP, MN, IIIB, RF, SF2 *HIV component:* gag, V3

- Virus-like particles could be formed from HIV-2 gag after deleting 143 amino acids at the C-terminal end – a proline rich region in positions 373-377 was critical to VLP formation
- CTL responses in BALB/c mice were induced by chimeric gag-V3 particles against the V3 region of HIV-1 clade B isolates IIIB (SIRIQRGRAFVTI), MN (KRIHIGPGRAFYTTK), RF (SITKGPGRVIYATGQ), and SF2 (SIYIGPGRAFHTTGR)
- The vaccine induced CTL were cross-reactive with a broad spectrum of B clade isolates, with the exception of the RF V3 which did not induce CTL

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gp160(308–322) gp160( ) RIHIGPGRAFYTTKN Vaccine human( ) [Pinto (1999)]

Vaccine: *Vector/type:* peptide *Strain:* MN *HIV component:* V3 *Stimulatory Agents:* Montanide ISA 51

- Epitope name: Peptide P18. Eight HIV+ individuals were vaccinated with peptides containing specific T helper, CTL and Ab epitopes in Montanide ISA 51 in a Phase I trial
- Four displayed a 4-fold increase in PCLUS 3-18 MN-specific T helper responses
- One patient developed a new, sustained P18MN-peptide-specific CTL response – the patient's HLA haplotype was A2,30; B53,7; Cw2,4, and anti-HLA A2 antibody did not inhibit the response, suggesting it was not A2
- Patients with low baseline Ab levels developed an increase of neutralizing Ab titers
- No significant change was observed in plasma HIV viral loads and CD4 cell counts

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gp160(308–322) gp120( ) RIHIGPGRAFYTTKN HIV-1 infection chimpanzee( ) [Lubeck (1997)]

- Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant
- CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK HIV-1 exposed seronegative human( ) [Pinto (1995)]

- CTL and T helper cell reactivity in healthcare workers exposed to HIV

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gp160(308–322) gp120(313–327 MN) RIHIGPGRAFYTTKN HIV-1 exposed seronegative human( ) [Pinto (1995)]

- CTL and T helper cell reactivity in healthcare workers exposed to HIV

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK Vaccine human(A11) [Achour (1994)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- One of 3 HLA type restrictions associated with this peptide

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gp160(308–322) gp120(315–329 BRU) RIQRGPGRAFVTIGK HIV-1 infection human(A2) [Dadaglio (1991)]

- Defined through blocking CTL activity, and Env deletions

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gp160(308–322) gp120(315–329 IIIB) RIQRGPGRAFVTIGK HIV-1 infection human(A2) [Clerici (1991)]

- Helper and cytotoxic T-cells can be stimulated by this peptide (P18)

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	human(A2, A3)	[Achour (1993)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- Two of 3 HLA type restrictions associated with this peptide

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(D^d)	[Takahashi (1989a)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3

- R(8) F(10) MHC/peptide interaction

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(D^d)	[Sastry (1992)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3

- Free peptide injected into the footpad of a mouse could stimulate specific CTL

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(D^d)	[Ahlers (1997b)]

Vaccine: *Vector/type:* peptide *Strain:* MN *HIV component:* V3

- PCLUS 3-18MN synthetic peptide vaccine construct contained T1 helper epitope covalently linked to truncated P18 CTL epitope
- A substitution in the T1 peptide stimulated an enhanced Th response and class II binding specificity, which in turn enhanced CTL induction by vaccine
- Construct PCLUS 3-18MN is currently in a phase I vaccine clinical trial

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gp160(308–322)	gp120(313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	murine(D^d)	[Takahashi (1989b)]

Vaccine: *Vector/type:* vaccinia *Strain:* MN, IIIB *HIV component:* gp160

- Y(11 MN) exchange with V(11 IIIB) interchanges specificities

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gp160(308–322)	gp120(313–327 IIIB MN RF)	SITKGPGRVIYATGQ	Vaccine	murine(D^d)	[Takahashi (1992)]

Vaccine: *Vector/type:* vaccinia *Strain:* RF *HIV component:* gp160

- Comparison of MN, IIIB, and RF specificities, position 11 is critical

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gp160(308–322)	gp120( )	RIQRGPGRAFVTIGK	Vaccine	murine(H-2^d)	[Deml (1997)]

Vaccine: *Vector/type:* virus-like particle *HIV component:* Gag, Env

- Env bound to virus-like particles (VLPs) can elicit a CTL response that is dependent on the amount of Env presented on the VLP

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gp160(308–322)	gp120(313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	murine BALB/c(H-2^d)	[Fomsgaard (1998a)]

Vaccine: *Vector/type:* DNA *Strain:* MN *HIV component:* gp160, V3

- Enhanced B and CTL responses to the V3 region occur following epidermal immunization by gene gun with a chimeric DNA vaccine of V3-hepatitis B surface antigen relative to a gp160 plasmid vaccine

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gp160(308–322)	gp120(313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	murine BALB/c(H-2^d)	[Ahlers (1996), Ahlers (1997a)]

Vaccine: *Vector/type:* peptide *Strain:* MN *HIV component:* V3 *Stimulatory Agents:* GMCSF, IL-12

- Vaccine constructs containing helper, antibody and CTL peptide epitopes induce strong Th1, CTL and NAb responses against the autologous HIV-1 virus
- The peptide CTL response was as cross-reactive as one elicited by a vaccinia construct expressing rgp160 MN
- GM-CSF and IL-12 were the two cytokines most effective for inducing and boosting CTLs

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(H-2^d)	[Layton (1993)]

Vaccine: *Vector/type:* virus-like particle *Strain:* IIIB *HIV component:* V3, Gag

- V3-Ty-Virus-like particles can induce type-specific CTL in mice in the absence of adjuvant

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(H-$2^{d,p,u,q}$)	[Shirai (1992), Shirai (1993)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: P18. In a murine system multiple class I molecules can present this peptide to CTL, including H-2D^d, H-2D^p, H-2D^q, H-2L^q
- The MHC class I molecule D^d as well as H-$2^{u,p,q}$, were found to present peptides P18 and HP53
- The V-β usage in T-cells showing cross-reaction between these two peptides was conserved for H-$2^{d,u,p}$, but not in H-2^q

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gp160(308–322)	gp160( )	GIHIGPGRAFYAARK	Vaccine	murine(H-2D^d)	[Morris (2000)]

Vaccine: *Vector/type:* recombinant protein, peptide *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* mucosal adjuvant LT(R192G)

- LT(R192G) induces gp160-specific serum and mucosal IgG1 and IgG2a, systemic CTL activity and Th1 and Th2 cytokine responses upon internasal immunization

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(H-2D^d)	[Porgador (1997)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3 *Stimulatory Agents:* cholera toxin adjuvant

- A intranasal peptide vaccine with cholera toxin as a mucosal adjuvant was given.
- IIIB peptide referred to as R15K
- Peptide-specific CTLs were induced after *in vitro* restimulation with peptide-pulsed targets
- R15K was superior at inducing CTL compared to the RGPGRAFVTI, in contrast to the findings of Nehete *et al*.
- Memory CTL responses were induced

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	(H-2D^d)	[Chiba (1999)]

Vaccine: *Vector/type:* vaccinia with H1 influenza HA gene cassette *Strain:* IIIB *HIV component:* P18

- Epitope name: P18. Vaccine was capable of priming P18IIIB specific CTL in BALB/c mice, but could not induce a P18IIIB-specific antibody response

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gp160(308–322)	gp120( )	RIHIGPGRAFYTTKN	Vaccine	murine(H-2D^d)	[Casement (1995)]

Vaccine: *Vector/type:* peptide *Strain:* MN, SC *HIV component:* V3

- Epitope name: P18. V3 peptides from MN and SC induce murine CTL that are cross-reactive with diverse strains

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gp160(308–322)	gp120(313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	murine(H-2D^d)	[Newman (1997)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp120 *Stimulatory Agents:* QS-21 adjuvant

- Epitope name: P18. MN vaccine induced CTL reactive with MN, IIIB and RF vaccinia-expressed Env, but not this peptide

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(H-2D^d)	[Newman (1997)]

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp120 *Stimulatory Agents:* QS-21 adjuvant

- Epitope name: P18. IIIB vaccine induced IIIB type-specific CTL to this peptide (P18), and an additional Env CTL response that was cross-reactive

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gp160(308–322)	gp120(315–329)	RIQRGPGRAFVTIGK	Vaccine	murine(H-2D^d)	[Takahashi (1988)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: P18. V3 loop CTL response in mice vaccinated with gp160

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gp160(308–322)	gp120(315–329)	RIQRGPGRAFVTIGK	Vaccine	murine BALB/c(H-2D^d)	[Fukasawa (1998)]

Vaccine: *Vector/type:* liposome *Strain:* IIIB *HIV component:* V3 *Stimulatory Agents:* oligomannose

- Epitope name: P18. The peptide RIQRGPGRAFVTIGK was incorporated into liposomes and given as a subcutaneous injection, which induces a MHC class I restricted CTL response in mice
- Liposomes coated with oligomannose show no toxicity and can elicit a potent CTL response upon a single subcutaneous infection, while non-coated liposomes do not, suggesting that oligomannose may be a good adjuvant for CTL responses

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gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(H-2D^{d,p,q}, H-2^u)	[Shirai (1996)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- Epitope name: P18. Multiple murine MHC can cross-present this epitope (P18) and HP53, DRVIEVVQGAYRAIR, to specific CTL

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gp160(308–322)	gp120( )	RIQRGPGRAFVTIGK	Vaccine	murine(H-2^d)	[Griffiths (1993)]

Vaccine: *Vector/type:* recombinant protein *HIV component:* Gag, V3

- Gag-V3 fusion protein immunization elicited V3 CTL response in mice

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gp160(308–322)	gp120( )	RIQRGPGRAFVTIGK	Vaccine	murine(H-2^d)	[Barouch (1998)]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* gp120 *Stimulatory Agents:* IL-2 or IL-2/Ig

- Epitope name: P18. A discistronic IL-2 gp120 expression vector gave a weaker CTL response than gp120 alone in the expression vector, however co-administration of an Il-2/IgG fusion protein enhanced the immune response and administration of a Il-2/IgG plasmid had a response that depended on the timing of administration.
- This study showed that a response to an HIV-1 DNA vaccine could be either augmented or suppressed by plasmid Cytokine/Ig administration

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gp160(308–322)	Env(308–322 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine(H-2^d)	[Uno-Furuta (2001)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3 loop *Stimulatory Agents: in vivo* electroporation, immunostimulatory sequence ISS, B7-1

- Epitope name: P18. Peptide immunization usually doesn't elicit a good CTL response because epitopes are not internalized and processed and presented, so vaccination with electric pulsing was tried (i.m. injection followed by 8 electric pulses), to enhance peptide uptake through electroporation
- BALB/c immunized with HIV P18 or hepatitis C P17 peptides with an electric pulse elicited a CTL response, those that did not receive the pulse did not
- The CTL response was enhanced by addition of immunostimulatory sequences ISS in the plasmid pCMV-LacZ, that contains hexamers GACGTC, AGCGCT, AACGCT, sequences common in prokaryotic genomes but rare in eukaryotic genomes that elicit Th1 cytokines and result in B cell and T-cell proliferation
- The CTL response was also enhanced by addition of B7-1 cDNA – the B7 family of proteins transduce co-stimulatory signals through interaction with CD28

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gp160(308–322)	gp160( )	RIHIGPGRAFYTTKN	Vaccine	murine BALB/c and C57/BL6(H-2^d and H-2^b)	[Fomsgaard (1998b)]

Vaccine: *Vector/type:* DNA *Strain:* MN *HIV component:* gp160

- CTL responses to a primary gene gun vaccination were rapid and strong for several methods of vaccinations: i.m., bupivacaine pretreatment, cardiotoxin pretreatment or gene gun – the CTL response was more rapid and consistent than the antibody response

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gp160(309–317)	gp120(310–318 SF2)	IYIGPGRAF	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402
- This peptide induced CTL in 1/4 HIV-1+ people tested
- IYIGPGRAF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – no specific CTL clones were obtained

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gp160(309–318)	gp120(314–323 CM243 CRF01)	ITVGPGQVFY	HIV-1 infection	human(A11)	[Sriwanthana (2001)]

- Epitope name: E309-318. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was strongly reactive in HIV+ control study subject 184 who carried HLA-A11

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gp160(309–318) gp120(314–323 CM243 CRF01) ITVGPGQVFY HIV-1 infection human(A11) [Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it
- This epitope was not conserved in other subtypes, and exact matches were rare

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gp160(310–318) Env(313–321) HIGPGRAFY HIV-1 infection human(A*3002) [Mulligan (2001)]

- Epitope name: E30. CTL response in Patient 07107 with HLA genotypes A*3002, A*3201, B*4501, B*5301, Cw*0401, Cw*1202

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gp160(310–323) gp120(315–328 MN) HIGPGRAFYTTKNI Vaccine murine(H-2D^d) [Arp (1999)]

Vaccine: *Vector/type:* canarypox prime with pseudovirion boost *Strain:* MN, IIIB *HIV component:* gp120, Gag, Pro

- Epitope name: p97. The vaccine vCP205, canarypox vector, MN gp120 + Gag/Pro IIIB, with an HIV-1 pseudovirion boost was given to mice;)
- HIV-1 pseudovirion boost enhanced the CTL response to this epitope in immunized BALB/c mice as measured by CTL lysis and IFNγ production

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gp160(311–319) gp120(312–320 SF2) IGPGRAFHT Vaccine murine(D^d) [Selby (1997)]

Vaccine: *Vector/type:* DNA *Strain:* SF2 *HIV component:* gp120

- Murine CTL response to peptide was observed after immunization with DNA plasmid containing HIV-1 (SF2) gp120 gene regulated by bacteriophage T7 promoter
- CTL response required coadministration of rec vaccinia virus expressing T7 RNA polymerase or T7 RNA polymerase soluble protein

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gp160(311–319) gp120( ) IGPGRAFHT Vaccine murine(H-2D^d) [Barnett (1997)]

Vaccine: *Vector/type:* DNA prime with rgp120 boost *Strain:* SF2 *HIV component:* gp120

- CTL were induced by vaccine, and restimulated *in vitro* with V3 peptide
- DNA vaccine with protein boost stimulated both CTL and antibodies
- Strains SF2 (IGPGRAFHT), US4 (IGPGRAFYA), and CM235 (IGPGQVFYR) were tested

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gp160(311–320) gp160(318–327 IIIB) RGPGRAFVTI Vaccine Macaca fuscata( ) [Okuda (1997)]

Vaccine: *Vector/type:* DNA prime with peptide boost *Strain:* IIIB *HIV component:* gp160, V3, CD4BS, HPG30

- Epitope name: P18. Murine BALB/c (H-2^d) and macaque both showed highest level of CTL vaccine response when a DNA vaccine was boosted with a peptide including four peptide subtypes of the V3 region, HPG-30 and a fragment of the CD4 binding region

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gp160(311–320) gp120(318–327) RGPGRAFVTI HIV-1 infection human( ) [Kmieciak (1998b)]

- Epitope name: P18. Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product
- This epitope doesn't have A2 anchors, but has features that confer promiscuous A2 binding, which may relate to the inhibitory effect seen in this paper

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gp160(311–320) Env( ) RGPGRAFVTI Vaccine murine BALB/c( ) [Lu (1999)]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* gp160, rev *Stimulatory Agents:* MIP-1α

- Epitope name: P18. MIP-1α co-inoculation increased IgG1/IgG2a ratio T-helper type 1 response.
- A MIP-1αexpression plasmid increased the CTL response to this DNA vaccine, as well as the T help response, presumably by the MIP-1αinteracting with T lymphocytes and macrophages

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gp160(311–320) gp160(318–327 IIIB) RGPGRAFVTI *in vitro* stimulation human(A*0201) [Alexander-Miller (1996)]

- Epitope name: P18. This eptiope stimulates a CTL line derived from an HIV negative donor.
- This immunogenic peptide does not have the known binding motif for A2.1
- The same optimal peptide for this human HLA-A2.1 epitope was observed for a murine H-2 D^d epitope

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gp160(311–320) gp120(311–320 IIIB) RGPGRAFVTI human(A*0201) [Brander & Goulder(2001)]

- Epitope name: P18. C. Brander notes this is an A*0201 epitope

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gp160(311–320) gp160(318–327 IIIB) RGPGRAFVTI Vaccine human(A2) [Achour (1996)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: P18. Individual was immunized with rec vaccinia gp160 IIIB and boosted with purified gp160
- Lysis only occurs with IIIB P18 peptide pulsed onto autologous targets; MN, RF, SIMI P18 peptides fail to stimulate CTL
- Restimulating immune cells from gp160 IIIB vaccinees with MN, RF, or SIMI P18 did not enhance the MN, RF, or SIMI specific CTL response

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gp160(311–320) gp160(318–327 SIMI) MGPKRAFYAT Vaccine human(A2) [Achour (1996)]

Vaccine: *Vector/type:* vaccinia prime with rgp160 boost *Strain:* SIMI *HIV component:* gp160

- Epitope name: P18. Individual was immunized with rec vaccinia gp160 SIMI and boosted with purified recombinant gp160 SIMI
- P18 MN and RF peptides were able to stimulate the HIV-specific CTL that arose in response to the SIMI vaccination, thus the P18 MN peptide (IGPGRAFYTT) and the P18 RF peptide (KGPGRVIYAT) could cross-react

- The P18 IIIB peptide does not cross-react (RGPGRAFVTI in the epitope region)
- gp160 SIMI primed immune cells could generate a significantly broader specificity when stimulated with P18 MN or P18RF peptides, but not P18 IIIB

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gp160(311–320) gp120(311–320) RGPGRAFVTI HIV-1 infection human(A2) [Day (2001)]

- Epitope name: P18. The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person

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gp160(311–320) gp160(318–327 IIIB) RGPGRAFVTI Vaccine murine(D) [Nehete (1995)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3 *Stimulatory Agents:* Freund's adjuvant

- Epitope name: P18. RGPGRAFVTI was defined as the optimal peptide for vaccination, out of RIQRGPGRAFVTIGK
- This peptide, in a carrier-free form in Freund's adjuvant, could stimulate Env specific CTL in BALB/c mice

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gp160(311–320) gp160(318–327 IIIB) RGPGRAFVTI Vaccine murine(D^d) [Takahashi (1993)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3

- Epitope name: P18. Successful priming with vaccination of peptide pulsed splenic dendritic cells

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gp160(311–320) gp160(318–327 IIIB) RGPGRAFVTI Vaccine murine(D^d) [Takahashi (1996)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3

- Epitope name: P18. Exposure of CD8+ CTL to free peptide corresponding to the epitope results in strong inhibition of the CTL response to targets presensitized with the same peptide
- The authors propose this is due to a "self-veto", where the CTL is inactivated by a CD8+ cell carrying the appropriate peptide-MHC complex

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gp160(311–320) Env(318–327) RGPGRAFVTI murine(H-2^d) [Lopez (2000)]

- Epitope name: P18. A series of protease and proteasome inhibitors was used to identify elements of the processing pathway of this epitope, called p18, both from within Env and from within a chimeric hepatitis B protein which allows proper processing
- Lactacystin, a proteasome inhibitor, partially inhibits endogenous processing of p18 epitope suggesting both a proteasome pathway and an additional pathway can be used
- Both TAP dependent and TAP-independent pathways can be used
- 1,10-phenanthrolin (metallopeptidases inhibitor) blocks epitope presentation demonstrating metalloproteinase processing in the Tap-dependent pathway
- The Tap-independent pathway does not involve processing by metalloproteinases
- This epitope is immunodominant in mice, and is presented by multiple human HLA alleles – it as been suggested that the high processing efficiency of this epitope might result in poor presentation of co-expressed epitopes

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gp160(311–320)	gp120( )	RGPGRAFVTI	Vaccine	murine(H-2^d)	[Hanke (1998a), Hanke (1998b)]

Vaccine: *Vector/type:* vaccinia *HIV component:* polyepitope

- Epitope name: P18. This murine epitope was incorporated into a vaccine of CTL epitopes expressed together including 20 HIV epitopes recognized by humans from 12 HLA types, one murine HIV epitope and three macaque HIV epitopes, delivered in a vaccinia virus Ankara (VVA) construct
- The murine vaccination was more effective at generating CTL when given i.v. rather than i.m.

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gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	Vaccine	murine BALB/c(H-2^d)	[Hamajima (1997)]

Vaccine: *Vector/type:* peptide *HIV component:* V3, HPG30, CD4BS *Stimulatory Agents:* IL-12

- Epitope name: P18. B cell epitope HGP-30 also serves as a CTL epitope
- Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide
- IL-12 expression plasmid included with the vaccination enhanced the CTL response

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gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	Vaccine	murine(H-2^d)	[Arai (2000)]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* 8 Br-cAMP/CMV promotor

- Epitope name: P18. Low-dosage 8 Br-cAMP given in combination with a DNA vaccine to BALB/c mice increased IgG and sIgA levels, and enhanced Th1, Th2 and CTL activity – the adjuvant activity may be mediated by activation of the CMV promotor in the DNA vaccine

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gp160(311–320)	gp120(318–327 IIIB)	RGPGRAFVTI	Vaccine	murine(H-2^d)	[Goletz (1997)]

Vaccine: *Vector/type:* fusion protein with anthrax delivery domain *HIV component:* gp120

- Epitope name: P18. Anthrax lethal toxin can deliver proteins to the cytosol of eukaryotic cells
- A fusion protein linking the delivery domain of the anthrax protein to gp120 achieved cellular uptake, and gp120 was processed allowing presentation of this V3 epitope to CTL *in vitro*

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gp160(311–320)	gp120(318–327 IIIB)	RGPGRAFVTI	Vaccine	murine(H-$2^{d,p,u}$)	[Shirai (1997)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: P18. Three class I MHC, H-$2^{d,p,u}$, that differ in sequence and serology, cross-present this peptide to T-cells of each of the other haplotypes
- The amino acids R, F, and I are each critical for strong CTL activity with all three MHC molecules

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gp160(311–320)	gp160( )	RGPGRAFVTI	Vaccine	murine(H-2^{d17})	[Hanke (1998a)]

Vaccine: *Vector/type:* vaccinia *HIV component:* polyepitope

- Epitope name: P18. Recombinant modified vaccinia virus Ankara (MVA) is an attenuated vaccinia that can not replicate in mammalian cells – strings of CTL epitopes were delivered and expressed in a MVA DNA vector

- γ IFN and CTL activity were induced after a single vaccination
- An MVA boost enhanced the response

gp160(311–320)	Env( )	IGPGRARYAR	Vaccine	murine BALB/c(H-2D)	[Belyakov (1998b)]

Vaccine: *Vector/type:* vaccinia *Strain:* 89.6 *HIV component:* gp160

- Epitope name: P18. Recombinant modified vaccinia virus Ankara (MVA), an attenuated vaccina which has lost the ability to replicate in mammalian cells, was used as the live vector for this vaccine study
- A single intrarectal mucosal immunization resulted in long lasting mucosal CTL responses and production of proinflammatory cytokines in mucosal sites, indicating that MVA was as effective in inducing mucosal CTL as replicating recombinant vaccinia

gp160(311–320)	Env( )	IGPGRARYAR	Vaccine	murine BALB/c(H-2D)	[Belyakov (1998a)]

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* V3

- Epitope name: P18. HIV protection and mucosal CTL response was studied – an HIV peptide immunogen could protect against gp160 expressing vaccinia in a murine intrarectal challenge system in which neutralizing Abs did not play a role, demonstrating mucosal CTL at the site of exposure can be protective

gp160(311–320)	gp120( )	IGPGRAFYTT	Vaccine	murine(H-2D^d)	[Lapham (1996)]

Vaccine: *Vector/type:* B. abortus-peptide conjugate

- Epitope name: P18. *B. abortus*-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice

gp160(311–320)	gp160( )	RGPGRAFVTI	Vaccine	murine(H-2D^d)	[Bruce (1999)]

Vaccine: *Vector/type:* non-replicating adenovirus *Strain:* IIIB *HIV component:* Env, Rev

- Epitope name: P18. A good HIV-1 Env immune response using non-replicating adenovirus vectors in BALB/c mice is dependent upon the presence of the stimulatory tat/rev 5'splice-donor site sequence and the presence of Rev
- Administration of monocistronic RAd501 expressing env and RAd46 expressing rev resulted in a positive CTL response, but required two immunizations for a CTL response comparable to that induced by the bicistronic virus RAd142
- Administration of RAd501 alone gave a low CTL response, but no humoral response, suggesting a lower level of antigen may be required to stimulate CTL

gp160(311–320)	gp120( )	IGPGRAFYTT	Vaccine	murine(H-2D^d)	[Lapham (1996)]

Vaccine: *Vector/type:* B. abortus-peptide conjugate

- Epitope name: P18. *B. abortus*-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice

gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	Peptide-HLA interaction	murine(H-2D^d)	[Takeshita (1995)]

- Epitope name: P18. XGPXRXXXXI are critical for binding, consistent with H-2D^d motif XGPX(RKH)XXX(X)(LIF)

gp160(311–320)	Env( )	RGPGRAFTVTI	Vaccine	murine(H-2D^d)	[Hanke & McMichael(1999), Hanke (1999)]

Vaccine: *Vector/type:* DNA/MVA boost *HIV component:* V3

- Epitope name: P18. Vaccinated mice elicited a CTL response to a gene gun-delivered multiepitope vaccine to two epitopes studied that are known to elicit CTL in mice: SYIPSAEKI from Plasmodium berghei and RGPGRAFTVTI from HIV-1 Env
- Different vaccination protocols were tested and it was found that a gene gun mediated delivery followed by an MVA boost was as good as i. m. immunization followed by a MVA boost – this is advantageous as gene gun delivery requires far less DNA than i.m. DNA priming
- CTL activity was high (60% - 70% specific lysis at effector target) when vaccinated with a single gene gun immunization and an MVA boost, and improved with two gene gun vaccinations

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gp160(311–320)	Env( )	RGPGRAFVTI	*in vitro* stimulation	murine(H-2Dd)	[Nakagawa (2000)]

- Epitope name: I-10. The CTL line LINE-IIIB was generated by repetitive restimulation of BALB/c spleen cells with vSC-25, IIIB gp160-expressing vaccinia
- RGPGRAFVTI represents the active minimal epitope within the previously described immunodominant epitope P18IIIB (RIQRGP-GRAFVTIGK, gp160(308-322)
- External processing of P18IIIB results in the removal of the 2 C-terminal residues (GK) of I-10 by ACE (angiotensin-1-converting-enzyme) in sera to produce I-10, and this processing is essential for target cell presentation of RIQRGPGRAFVTIGK

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gp160(311–320)	gp160( )	RGPGRAFVTI	Vaccine	murine(H-2^d)	[Gherardi (2000)]

Vaccine: *Vector/type:* DNA, vaccinia *HIV component:* env *Stimulatory Agents:* IL-12

- Epitope name: P18. Induction of HIV-1 specific CD8 γ IFN secreting cells was enhanced when IL-12 and Env were given together in a prime, followed by a VV expressing Env boost
- If IL-12 was also delivered as a boost from the viral vector, impairment of the IL-12 effects was noted, indicating that the vaccination schedule can be a critical parameter for success with DNA and vaccinia vectors used in combination with immunomodulators
- The negative effect observed when IL-12 was delivered with the boost involved nitric oxide

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gp160(311–320)	Env( )	RGPGRAFVTI	Vaccine	murine(H-2^d)	[Xin (1999)]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* gp160, rev *Stimulatory Agents:* IL-15 and IL-2, IL-12

- Epitope name: P18. A study of the DNA vaccine pCMV160IIIB/REV with IL-15 and IL-2 or IL-12 expression plasmids.
- Intranasal immunization of BALB/c mice with HIV DNA and IL-15 plasmid induced increased Th1 and CTL responses
- Co-administration of IL-15 with IL-12 or IL-2 plasmids did not alter the effect of IL-15
- Both the CTL (peptide pulsed targets) and DTH response (injection of peptide into footpad) to this peptide was monitored
- The Ab response to NNTRKSIRIQRGPGRAFVTIGKIGN was monitored, and IL-15 co-administration resulted in a decrease in the IgG1/IgG2a ratio

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gp160(311–320)	Env( )	RGPGRAFVTI	Vaccine	murine(H-2^d)	[Villacres & Bergmann(1999)]

Vaccine: *Vector/type:* vaccinia, Sindbis *HIV component:* V3

- Epitope name: P18. HIV-1 epitope p18 was expressed in two different vaccine vectors and the CTL response was compared in BALB/c mice
- Class I tetramer staining showed that up to 13% of the CD8+ splenocytes were p18 specific in the acute response using vaccinia, only 4% using Sindbis
- vp18 had more γ IFN secreting splenocytes and activated CD4+ and CD8+ T-cells
- The overall decline in CD8+ T-cells in the transition into memory was 2-3 fold for both vectors
- Sindbis virus recombinants induced protective memory cytotoxic T-cells, although reduced quantitatively, without vaccinia associated inflamation and replication

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gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	*in vitro* stimulation	murine(H-2^d)	[Takahashi (2001)]

- Epitope name: I-10. Pre-incubation of HIV-1 (IIIB) gp160 specific CTL with peptide without APCs reduced cytolytic activity 3.5 fold and induced peptide concentration dependent IL-2 unresponsiveness that might be due to IL-2Rβ down regulation
- An enhanced cytolytic activity was observed by addition of anti-IFN-γ, TNF-α or MIP-1β to I-10 suppressed CTLs

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gp160(311–320)	gp160( )	RGPGRAFVTI	Vaccine	murine(H-2^d)	[Shirai (2001)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: P18. *Helicobacter pylori* induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori

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gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	Vaccine	murine(L^d)	[Tobery & Siliciano(1997)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* env, nef

- Epitope name: P18. An HIV-1 Env vaccine was targeted for rapid cytoplasmic degradation
- The rapidly degraded form rapidly stimulated CTL to this peptide, faster than the normal vaccinia-env
- The rapidly degraded form also stimulated greater specific CTL lysis and higher CTLp frequencies than normal Env
- Similar results were obtained for a Nef protein designed for rapid degradation

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gp160(314–322)	gp120(314–322)	GRAFVTIGK	Peptide-HLA interaction	human(B27)	[Jardetzky (1991)]

- Study of peptide binding to HLA-B27

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gp160(337–361)	gp120(337–368 LAI)	KWNNTLKQIDSKLRE-QFGNNKTIIF	Vaccine	human(CD4+ CTL)	[Johnson (1994a)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- CD4+ CTL clones were obtained from an HIV-1 vaccinia-env vaccinee

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gp160(339–354)	gp120(339–361 LAI)	NNTLKQIDSKLREQFG	Vaccine	human(CD4+ CTL)	[Johnson (1994b)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- CD4+ CTL isolated from LAI IIIB gp160 vaccinees

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gp160(340–348)	gp120(346–354 CM243 CRF01)	RVLKQVTEK	HIV-1 infection	human(A11)	[Sriwanthana (2001)]

- Epitope name: E340-348. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was weakly reactive in HIV+ control study subject 053 who carried HLA-A11

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gp160(340–348)	gp120(346–354 CM243 CRF01)	RVLKQVTEK	HIV-1 infection	human(A11)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it
- This epitope was not conserved in other subtypes, and exact matches were rare

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gp160(340–349)	gp120( )	NTLKQIVIKL	Vaccine	chimpanzee(Patr-B*14)	[Balla-Jhagjhoorsingh (1999a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* W6.ID *HIV component:* gp120

- An HIV-1 rgp120 vaccine induced strong humoral and cellular immune response in sibling chimpanzees, but only one of the two made a detectable CTL response to this Patr-B*14 restricted immunodominant epitope

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gp160(369–375)	gp120(374–380 BRU)	PEIVTHS	HIV-1 infection	human(A2)	[Dadaglio (1991)]

- Defined through blocking CTL activity, and Env deletions

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gp160(375–383)	gp120(379–387 LAI)	SFNCGGEFF	HIV-1 infection	human(B*1516)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*1516 epitope

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gp160(375–383)	gp120(375–383 IIIB)	SFTCGGEFF	HIV-1 infection	human(B15)	[Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- An additional variant that gave a positive, though reduced, CTL response: SSTCGGEFF and SFTCGGGFF
- SFTCGGGVF was an escape mutant

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gp160(375–383)	gp120(375–383 SF2)	SFNCGGEFF	HIV-1 infection	human(B15)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B15+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/1 group 3

gp160(375–383)	gp120(375–383 IIIB)	SFNCGGEFF	HIV-1 infection	human(B63,B15)	[Wilson (1997)]

- This is the optimal peptide for two CTL clones that recognize this epitope in the context of two different HLA molecules, Cw4 and B15
- Predominant form in proviral DNA of the individual with B15 restricted CTL was SFTCGGEFF and this was recognized
- Recognition of a minor autologous variant (SFNCRGEFF) from the B15 donor was greatly reduced

gp160(375–383)	gp120(376–383 PV22)	SFNCGGEFF	HIV-1 infection	human(C*0401)	[Brander & Goulder(2001)]

- C. Brander notes this is a C*0401 epitope

gp160(375–383)	gp120(376–383 PV22)	SFNCGGEFF	HIV-1 infection	human(Cw4)	[Johnson (1993)]

- Conserved epitope

gp160(375–383)	gp120(376–383 PV22)	SFNCGGEFF	HIV-1 infection	human(Cw4)	[Wolinsky (1996)]

- Longitudinal study of epitope variation *in vivo*

gp160(375–383)	gp120(376–383)	SFNCGGEFF	HIV-1 exposed seronegative, HIV-1 infection	human(Cw4)	[Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-Cw4 women, 1/2 HEPS and 10/11 HIV-1-infected women recognized this epitope
- The dominant response to this HLA allele was to this epitope in 6 of the 10/11 responsive HIV-1-infected women, and not in the HEPS case

gp160(376–383)	gp120( )	FNCGGEFF		human(Cw4)	[Rowland-Jones (1999)]

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no δ32 deletion in CCR5
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive,
- HIV-2 sequence: TNCRGEFL – no cross-reactivity [Johnson (1993)]

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gp160(376–384)	gp120(376–384 IIIB)	FNCGGEFFY	HIV-1 infection	human(A29)	[Wilson (1997)]

- This is the optimal peptide for two CTL clones derived from two different donors
- FNCRGEFFY and FNCRGGFFY are major and minor autologous variants in one of the donors, and showed reduced or no stimulatory activity for CTL from the host
- The IIIB form and the form FNCAGEFFY were present in the other donor, and the CTL line had reduced activity with the FNCAGEFFY form relative to the index peptide

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gp160(376–384)	gp120(376–384 IIIB)	PNCGGEFFY	HIV-1 infection	human(A29)	[Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- PNCRGEFFY was an escape variant

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gp160(376–384)	gp120(376–384 LAI)	FNCGGEFFY	HIV-1 infection	human(A29)	[Mollet (2000)]

- Epitope name: E2. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

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gp160(376–384)	gp120(376–384)	FNCGGEFFY	HIV-1 infection	human(B8)	[Oxenius (2000)]

- Epitope name: FNC. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable
- One of the 7/8 study subjects that were HLA B8 recognized this CTL epitope
- Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197

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gp160(376–387)	gp120(381–392 BRU)	KNCGGEFFYCNS	HIV-1 infection	human(A2)	[Dadaglio (1991)]

- Defined through blocking CTL activity, and Env deletions

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gp160(377–387)	gp120(377–387)	NSGGEFFYSNS		human(A2)	[Hickling (1990)]
• Peptides recognized by class I restricted CTL can bind to class II					
gp160(383–391)	gp120(385–393)	FYCNTTQLF	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402					
• This peptide induced CTL in 1/4 HIV-1+ people tested					
• FYCNTTQLF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained					
gp160(410–429)	gp120(410–429 PV22)	GSDTITLPCRIKQFINM-WQE	*in vitro* stimulation	human(CD4+DRA)	[Bouhdoud (2000)]
• CTL were studied through PBMC stimulation *in vitro* by gp120 pulsed autologous monocytes.					
• Human CD4+ CTL clone (Een217) is an MHC class II HLA-DRA restricted CTL clone that can lyse antigen presenting HLA-DRA-transfected murine L cells – natural variants of the epitope resulted in an anergic response					
• Low concentrations of the HXB2-derived variant (GSDTITLPCRIKQIINMWQK) induced T-cell anergy – higher concentrations could induce proliferation and cytotoxic activity					
• CDC42 (TGDIITLPCRIKQII-NRWQV), Eli (TNTNITLQCRIKQIIKMVAG) and Z3 (CTGNITLPCRIKQIIMNWQE) variants did not induce proliferation, cytotoxic or anergic responses					
gp160(416–424)	Env(413–421 SF2)	LPCRIKQII	HIV-1 infection	human(B*5101)	[Tomiyama (1999)]
• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)					
• 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%					
• Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed					
• Four of the six epitopes were highly conserved among B subtype sequences, LPCRIKQII is not conserved					
gp160(416–424)	gp160(416–424 LAI)	LPCRIKQII		human(B*5101)	[Brander & Goulder(2001)]
• C. Brander notes this is a B*5101 epitope					
gp160(416–424)	gp120(378–385)	LPCRIKQII	HIV-1 exposed seronegative, HIV-1 infection	human(B51)	[Kaul (2001a)]
• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers					
gp160(416–429)	gp120(410–429 H3DCG)	LPCRIKQFINMWQE	HIV-1 infection	human(DR4 CD4+)	[Siliciano (1988)]
• CD4+ CTL restricted by class II HLA-DR4, targets primed by CD4 mediated uptake of gp120					

gp160(416–435)	gp120(421–440 LAI)	LPCRIKQFINMWQEV-GKAMY	HIV-1 infection	human(A2)	[Dadaglio (1991)]
• Defined through blocking CTL activity, and Env deletions					
gp160(419–427)	gp120(419–427 HXB2)	RIKQIINMW		human(A*3201)	[Harrer (1996b), Brander & Goulder(2001)]
• C. Brander notes this is an A*3201 epitope					
gp160(419–427)	gp120(419–427)	RIKQIINMW?	HIV-1 infection	human(A29, A32)	[Betts (2000)]
• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes • 1/11 of the A2+ individuals was A29 and responded to RIKQIINMW, and another responder was A32 and these are thought to be presenting molecules • The sequence is unclear – Betts calls both peptide 30 and peptide 32 gp120 419–427 and the peptide sequences are not provided					
gp160(419–427)	gp120(424–432 LAI)	RIKQFINMW	HIV-1 infection	human(A32)	[Ray (1998)]
• Autologous virus was used to detect CTL in two individuals, and in both cases strain-specific autologous CTL were found • The autologous epitope sequence was RIKQIINMW, MN and RF were KIKQFINMW and RIKQFVNMW respectively, and all were reactive with CTL clones					
gp160(419–427)	gp120(420–428)	RIKQIINMW	HIV-1 infection	human(A32)	[Ferris (1999)]
• This epitope is processed by a TAP1/2 dependent mechanism					
gp160(421–435)	gp120(421–440 LAI)	KQFINMWQEVGKAMY	HIV-1 infection	human(A2)	[Dadaglio (1991)]
• Defined through blocking CTL activity, and Env deletions					
gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMY-A	HIV-1 exposed seronegative	human( )	[Pinto (1995)]
• CTL and T helper cell reactivity in healthcare workers exposed to HIV					
gp160(421–436)	gp120( )	KQIINMWQEVGKAMY-A	HIV-1 infection	chimpanzee( )	[Lubeck (1997)]
• Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant • CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies • Helper and cytotoxic T-cells can be stimulated by this peptide (T1)					
gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMY-A	HIV-1 infection	human(A2)	[Clerici (1991)]
• Helper and cytotoxic T-cells can be stimulated by this peptide (T1)					

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMY-A	HIV-1 infection	human(A2)	[Cease (1987)]

- Helper and cytotoxic T-cells can be stimulated by this peptide (T1)

gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMY-A	Vaccine	murine(H-$2^{a,b,f}$)	[Shirai (1992)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- In a murine system multiple class I molecules can present to CTL

gp160(432–451)	gp120(439–458 IIIB)	KAMYAPPISGQIRCSS-NITG	Vaccine	Rhesus macaque( )	[Wagner (1998b)]

Vaccine: *Vector/type:* virus-like particle *HIV component:* gag, gp120, V3, CD4BS

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock
- CTL specific for this epitope could be found both before and after SHIV challenge

gp160(434–443)	gp120(431–440)	MYAPPIGGQI	Vaccine	murine(H-$2K^d$)	[Duarte (1996)]

Vaccine: *Vector/type:* peptide

- Tolerization of CTL response with continued administration of soluble peptide

gp160(435–443)	Env( )	YAPPISGQI	Vaccine	Rhesus macaque( )	[Barouch (2000), Shen & Siliciano(2000)]

Vaccine: *Vector/type:* DNA *Strain:* 89.6 *HIV component:* SIVmac239 Gag and HIV-1 89.6P Env *Stimulatory Agents:* IL-2/Ig

- Epitope name: p41A. Monkeys that received the DNA vaccines augmented with IL-2/Ig were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, stable CD4+ T-cell counts, preserved virus-specific CD4+ T-cell responses, low to undetectable viral loads, and no evidence of disease or mortality by day 140 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and were half were dead by day 140
- IL-2/Ig consisting of interleukin-2 (IL-2) for immune stimulation, and the Fc portion of immunoglobulin G (IgG) for stability, was delivered either as protein or as DNA – both enhance the CTL response to vaccination, DNA IL-2/Ig giving the most intense response
- Responses to a dominant Mamu A*01 gag epitope SIV Gag p11C (CTPYDINQM) and a subdominant epitope HIV-1 Env p41A (YAPPISGQI) were tracked and had good durability prior to challenge, and the higher the prechallenge peak p11C CTL response, the lower the post-challenge viral load
- No NAb responses were detected in the vaccinated monkeys prior to challenge, and comparable peak NAb titers developed in vaccinated monkeys and control monkeys with preserved CD4+ T-cells
- Shen *et al*. 2000 is an accompanying commentary

gp160(435–443)	Env( )	YAPPISGQI	Vaccine	Rhesus macaque( )	[Barouch (2001b)]

Vaccine: *Vector/type:* vaccinia *Strain:* 89.6 *HIV component:* SIVmac239 Gag/Pol and HIV-1 89.6P Env *Stimulatory Agents:* IL-2/Ig

- Epitope name: p41A. Four monkeys were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL to the immunodominant SIV gag eptiope in 4/4 animals, and 1/4 made a response to the HIV Env epitope YAPPISGQI, as determined by tetramer staining and chromium release assays
- The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168

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gp160(435–443)	( )	YAPPISGQI	SHIV infection	Rhesus macaque (Mamu A*01)	[Egan (1999)]

- SHIV-infected rhesus macaques have high frequencies of response to the SIVmac epitope gag p11C,C-M (CTPYDINQM) but only a fraction of A*01 monkeys tested have responses to SIVmac pol epitope STPPLVRLV and HIV-1 env epitope YAPPISGQI

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gp160(435–443)	gp41( )	YAPPISGQI	SHIV infection, Vaccine	Rhesus macaque (Mamu A*01)	[Barouch (2001a)]

Vaccine: *Vector/type:* vaccinia MVA, DNA *Strain:* 89.6, HXBc2 *HIV component:* SIV Gag and HIV-1 Env *Stimulatory Agents:* IL-2/Ig

- Epitope name: p41A. Mamu-A*01+ rhesus monkeys infected with SHIV-89.6 and SHIV-HXBc2 make immunodominant responses to SIV Gag p11C epitope (CTPYDINQM) and a subdominant response to HIV-1 Env p41A epitope (YAPPISGQI)
- The binding affinities are the same for the two epitopes to Mamu A*01, so that is not what dictates the dominance
- Monkeys vaccinated with MVA vectors carrying SIV gag/pol and HIV-1 env showed the same p11C epitope dominance and p41A epitope subdominance, but co-dominance was observed and the response to p41A increased when DNA vaccination was done using the SIV and HIV genes under CMV promotor control with IL-2-Ig adjuvant

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gp160(444–453)	Env( )	RCSSNITGLL		human(B56)	[De Groot (2001)]

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay
- RCSSNITGLL was newly-defined as an epitope in this study, and was shown to stimulate an ELISPOT response, despite not detectably binding to HLA-B7

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gp160(489–508)	gp120(494–513 BRU)	VKIEPLGVAPTKAKRR-VVQR	HIV-1 infection	human(A2)	[Dadaglio (1991)]

- Defined through blocking CTL activity, and Env deletions

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gp160(519–543)	gp41(519–543)	FLGFLGAAGSTMGAA-SLTLTVQARC	HIV-1 infection	human(Cw7)	[Nehete (1998)]

- Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one
- HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B
- HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T-cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing

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gp160(557–565)	gp41(557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human( )	[Wilson (1996)]

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study
- RAIDAQQHL and RVIEAQQHL, naturally occurring variants, were found in the mother and are recognized

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gp160(557–565)	gp41(557–565)	RAIEAQQHL	HIV-1 infection	human( )	[Betts (2000)]

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant
- Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes
- 1/11 of the A2+ individuals was HLA A*0201, A32, B60, B78, and responded to RAIEAQQHL, previously noted to be B51

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gp160(557–565)	gp41(557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human(B*5101)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*5101 epitope

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gp160(557–565)	gp41(557–665)	RAIEAQQWQ	HIV-1 infection	human(B*5101)	[Samri (2000)]

- Epitope name: E3. The epitope was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition

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gp160(557–565)	gp41(557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human(B15)	[Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- This epitope was invariant in both the mother and her infant

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gp160(557–565)	gp41(557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human(B51)	[Sipsas (1997)]

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB
- KAIEAQQHL, a variant found in HIV-1 NY5CG, was also recognized
- RAIEAQQHM, a variant found in HIV-1 JRCSF, was also recognized
- RAIDAQQHL, a variant found in HIV-1 ETR, was also recognized
- RAIKAQQHL, a variant found in HIV-1 CDC42, was also recognized

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gp160(557–565)	gp41(557–565)	RAIEAQQHL	HIV-1 infection	human(B51)	[Ferris (1999)]

- This epitope can be processed by a TAP1/2 dependent mechanism

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gp160(557–565)	gp41(557–565)	RAIEAQQWQ	HIV-1 infection	human(B51)	[Oxenius (2000)]

- Epitope name: RAI. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable
- None of the 8 study subjects recognized this epitope but none were HLA B51+

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gp160(557–565)	gp41(47–55)	RAIEAQQHL	HIV-1 infection	human(B51)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

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gp160(557–565)	gp41(557–565 LAI)	RAIEAQQHL	HIV-1 infection	human(B51)	[Mollet (2000)]

- Epitope name: E3. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

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gp160(565–573)	Env(731–739)	LLQLTVWGI	HIV-1 infection	human(A2 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype), while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)

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gp160(565–573)	Env(731–739)	KLVGKLNWA	HIV-1 infection	human(A2 supertype)	[Propato (2001)]

- Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype), while the effector cells of long-term non-progressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)
- Tetramer staining with A2, β2-microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific cells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population

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gp160(570–589)	gp41(571–590 LAI)	VWGIKQLQARILAVER-YLKD	Vaccine	human(CD4+ CTL(DR-1))	[Kent (1997a)]

Vaccine: *Vector/type:* vaccinia prime with rgp160 boost *Strain:* LAI *HIV component:* gp160

- VWGIKQLQARILAVERYLKD, present in HIV-1 LAI, was the immunizing strain
- VWGIKQLQARVLAVERYLKD, present in HIV-1 MN, was also recognized
- VWGIKQPQARVLAVERYLRD was the form carried by the autologous strain that infected the vaccinee
- Lysis of the target cells by CD4+ CTL was inhibited with the addition of the peptide representing the autologous strain
- The infecting virus epitope also antagonized the proliferative functions of the CD4+ CTL clone
- The behavior of the autologous strain presents a possible mechanism for vaccine failure since the infecting virus not only escapes CTL activity, but inhibits the ability of CTL to recognize other variants

gp160(572–590)	gp41(572–590 BRU)	GIKQLQARILAVERYL-KDQ	Vaccine	human(DPw4.2)	[Hammond (1991)]

Vaccine: *Vector/type:* recombinant protein *Strain:* BRU *HIV component:* gp160

- CD4+ CTL

gp160(575–599)	gp41(575–599 IIIB)	QLQARILAVERYLKDQ-QLLGIWGCS	HIV-1 infection	human(B14)	[Jassoy (1992)]

- Epitope recognized by CTL clone derived from CSF

gp160(583–592)	gp41(583–592 PV22)	VERYLKDQQL	HIV-1 infection	human(B14)	[Jassoy (1993)]

- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF

gp160(584–592)	gp41(589–597 SF2)	ERYLKDQQL	HIV-1 infection	human(B14)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3

gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human( )	[Price (1995)]

- Study of cytokines released by HIV-1 specific activated CTL

gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human( )	[Borrow (1994)]

- Three out of five patients with HIV-1 symptomatic infection controlled their viral infection well and mounted an early, strong HIV-1 specific MHC restricted CTL response
- One of the three, study subject BORI, specifically recognized this peptide

gp160(584–592)	gp41(584–592 HXB2)	ERYLKDQQL	HIV-1 infection	human(A32, B14)	[Mollet (2000)]

- Epitope name: E4. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

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gp160(584–592)	gp41(584–592 PV22)	ERYLKDQQL	HIV-1 infection	human(B*1402)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*1402 epitope

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gp160(584–592)	gp41( )	ERYLKDQQL	HIV-1 infection	human(B14)	[Wagner (1998a)]

- CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules

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gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Kalams (1999b)]

- Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV *in vivo* activated specific CTL such that by day 260 CTL activities were undetectable
- ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant
- Sporadic breakthrough in viremia resulted in increases in CTLp
- Peptide-tetramer staining demonstrated that declining levels of *in vivo*-activated CTL were associated with a decrease in expression of CD38
- Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load

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gp160(584–592)	gp41(591–599 SF2)	ERYLKDQQL	HIV-1 infection	human(B14)	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- One of these 11 had CTL response to this peptide
- The responding subject was HLA-A3, -A32, -B7, -B14

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gp160(584–592)	gp41(591–599 SF2)	ERYLKDQQL	HIV-1 infection	human(B14)	[Cao (1997)]

- The consensus sequence for clades B, C, and D is ERYLKDQQL
- The consensus sequence for clade A is ERYLRDQQL and it is equally reactive
- The consensus sequence for clade E is ERYLKDQKF and it is not reactive

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gp160(584–592)	gp41( )	ERYLKDQQL	HIV-1 exposed seronegative	human(B14)	[Rowland-Jones (1998a)]

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating
- The A and D subtype consensus are identical to the B clade epitope, ERyLkDQQL

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gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Sipsas (1997)]

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB

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gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Yang (1996)]

- CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL
- Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones
- The distinction was thought to be due to lower expression of RT relative to Env and Gag
- CTL can lyse infected cells early after infection, possibly prior to viral production

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gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Yang (1997a)]

- CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*
- CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation
- CTL suppress HIV replication more efficiently in HLA-matched cells

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gp160(584–592)	gp41(584–592 PV22)	ERYLKDQQL	HIV-1 infection	human(B14)	[Johnson (1992)]

- Two overlapping CTL epitopes were mapped with different HLA restriction (also see YLKDQQLL HLA-B8)

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gp160(584–592)	gp41(584–592 PV22)	ERYLKDQQL	HIV-1 infection	human(B14)	[Jassoy (1993)]

- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF

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gp160(584–592)	gp41(584–592 HXB2)	ERYLKDQQL	HIV-1 infection	human(B14)	[Kalams (1994), Kalams (1996)]

- Longitudinal study of T-cell receptor usage in a single individual
- Persistence of oligoclonal response to this epitope for over 5 years

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gp160(584–592)	gp41(584–592)	ERYLKDQQL	Peptide-HLA interaction	human(B14)	[DiBrino (1994a)]

- Epitope studied in the context of HLA-B14 binding

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gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Hammond (1995)]

- This peptide can be processed for HLA-B14 presentation in a TAP-1/2 independent pathway

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gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Kalams (1996)]

- CTL response to this epitope was studied in 5 HLA-B14 positive persons
- CTL responses were detected in all five, and CTL clones were isolated from 4/5

- A diverse repertoire of TCRs recognized this epitope, with similar fine specificities
- 3/5 subjects showed no variation in viral sequence, 2/5 had a dominant variant that resulted in poor recognition, ERYLQDQQL
- A minor CTL response specific for the ERYLQDQQL could be detected by two individuals, but the major CTL response was to the ERYLKDQQL form even when it was the minority form
- Some single amino acid substitutions were well tolerated by most of the CTL clones tested, but others, particularly in the center three amino acid positions, abrogated peptide stimulatory activity

gp160(584–592)	gp120(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Ferris (1999), Hammond (1995)]

- This epitope is processed by both TAP1/2 dependent and independent mechanisms

gp160(584–592)	gp41( )	ERYLKDQQL		human(B14)	[Rowland-Jones (1999)]

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no δ32 deletion in CCR5
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective
- HIV-2 sequence: EKYLQDQAR – no cross-reactivity [Johnson (1992)]

gp160(584–592)	gp41( )	ERYLKDQQL	HIV-1 infection	human(B14)	[Goulder (2001b)]

- Epitope name: EL9. Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia
- A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation
- Recognized by two A*0201-positive chronically infected subjects

gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Islam (2001)]

- Epitope name: 588K. Transcript frequencies of four CTL clones from patient 115, with a chronic and stable HIV-1 infection, were tracked in a longitudinal study of samples collected 6-11 years post infection: clones M21 and E15 recognize ERYLKDQQL, clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL
- CTL clone M21 uses the Vβ 4, CDR3 VKDGA, Jβ 1.2 TCR β gene, and clone E15 uses the Vβ 4, CDR3 VEDWGGAS Jβ 2.1 TCR β gene, and D87 uses Vβ8, ALNRVD, Jβ2.1
- Responses were stable even through HAART with undetectable viral loads but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time

gp160(584–592)	gp41(589–597)	ERYLRDQQL	HIV-1 exposed seronegative, HIV-1 infection	human(B14)	[Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

gp160(584–592)	gp41( )	ERYLKDQQL	HIV-1 infection	human(B14)	[Severino (2000)]

- Primary HLA-B14+ CD4+ CD3+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the B14-restricted CTL clone 15160/D75 specific for ERYLKDQQL, and viral inhibition was MHC-restricted
- Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL
- DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture

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gp160(584–592) gp41( ) ERYLKQQL HIV-1 infection human(B14) [Altfeld (2000)]

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by a molecule other than B60 in an HLA-B60 individual

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gp160(584–592) gp41( ) ERYLKDQQL HIV-1 exposed seronegative human(B14, B*1402) [Rowland-Jones (1998b)]

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes
- This epitope is conserved among B and D clade viruses
- The clade A version of the epitope is ERYLRDQQL

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gp160(585–592) gp41(584–591 SF2) RYLRDQQL HIV-1 infection human(A*2402) [Ikeda-Moore (1997)]

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402
- This peptide induced CTL in 2/4 HIV-1+ people tested
- RYLRDQQL bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained

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gp160(585–592) gp41(590–597 LAI) RYLKDQQL HIV-1 infection human(B27) [Shankar (1996)]

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gp160(585–593) gp41(584–591 SF2) RYLRDQQLL HIV-1 infection human(A*2402) [Ikeda-Moore (1997)]

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402
- This peptide induced CTL in 4/4 HIV-1+ people tested
- RYLRDQQLL bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained

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gp160(585–593) gp41(591–598 LAI) RYLKDQQLL human(A*2402) [Brander & Goulder(2001)]

- C. Brander notes this is an A*2402 epitope

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gp160(585–595) gp41(584–591 SF2) RYLRDQQLLGI HIV-1 infection human(A*2402) [Ikeda-Moore (1997)]

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402

- This peptide induced CTL in 4/4 HIV-1+ people tested
- RYLRDQQLLGI bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained

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gp160(586–593) gp160( ) YLRDQQLL HIV-1 infection human( ) [Kaul (2001b)]

- This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative
- The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire
- This epitope was recognized in 1/22 HEPS sex worker controls, ML887

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gp160(586–593) gp41(584–591 NL43) YLKDQQLL HIV-1 infection human(A*2402) [Dai (1992)]

- The lysine (K) is critical for eliciting a HLA-A24 CTL response
- C. Brander notes that this is an A*2402 epitope in the 1999 database, and suggested that the epitope is RYLKQQLL

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gp160(586–593) gp41(591–598) YLRDQQLL HIV-1 exposed seronegative, HIV-1 infection human(A24) [Kaul (2001a)]

- Variants (R)YL(R/K)DQQLL are specific for the A/B clade
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-A24 women, 3/4 HEPS and 10/10 HIV-1-infected women recognized this epitope, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only
- The dominant response to this HLA allele was to this epitope in all 3/4 HEPS cases but in only 4 of the 10/10 HIV-1-infected women
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort

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gp160(586–593) gp41(580–587 CM243 CRF01) YLKDQQLL HIV-1 infection human(A24) [Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested
- The only HLA-A24 FSW tested did not recognized the E clade version of this epitope RYLKDQKLL, which differs from the previously defined B clade version by one amino acid, YLKDQQLL, with an additional amino acid added on

- This epitope was only conserved in CRF01 (subtype E), and identities were rare

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gp160(586–593) gp41(586–593 LAI) YLKDQQLL HIV-1 infection human(A24,B8) [Mollet (2000)]

- Epitope name: E1. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

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gp160(586–593) gp41(586–593) YLKDQQLL HIV-1 infection human(B*0801) [Brander & Goulder(2001)]

- C. Brander notes this is a B*0801 epitope

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gp160(586–593) gp41(586–593) YLKDQQLL HIV-1 infection human(B8) [Johnson (1992)]

- Two overlapping CTL epitopes were mapped with different HLA restriction (also see ERYLKDQQL HLA-B14)

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gp160(586–593) gp41(586–593) YLKDQQLL Peptide-HLA interaction human(B8) [Sutton (1993)]

- Predicted epitope based on B8-binding motifs, from larger peptide QLQARILAVERYLKDQQLLGIWGCS

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gp160(586–593) gp41(76–83) YLKDQQLL human(B8) [Goulder (1997g)]

- Included in a study of the B8 binding motif

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gp160(586–593) gp41( ) YLKDQQLL human(B8) [Rowland-Jones (1999)]

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no δ32 deletion in CCR5
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive
- HIV-2 sequence: YLQDQARL – no cross-reactivity [Johnson (1992)]

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gp160(586–593) gp41(586–593) YLKDQQLL HIV-1 exposed seronegative, HIV-1 infection human(B8) [Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

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gp160(586–593) gp41(586–593) YLKDQQLL HIV-1 infection human(B8) [Day (2001)]

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual

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gp160(586–598) gp41(586–598) YLRDQQLLGIWGC HIV-1 infection human(Cw7) [Nehete (1998)]

- Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one
- HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B

- HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T-cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing

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gp160(594–608) gp41( ) GIWGCSGKLICTTAV HIV-1 infection human(B57) [Jin (1998b)]

- Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction
- Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK

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gp160(606–614) gp41(605–615 LAI) TAVPWNASW Vaccine human(B*3501) [Brander & Goulder(2001)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- C. Brander notes this is a B*3501 epitope

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gp160(606–614) gp41(606–614 HXB2) TAVPWNASW HIV-1 infection human(B*3501) [Ferris (1996)]

- Natural form of this peptide is not glycosylated, suggesting initial Class I processing may occur in the cytosol

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gp160(606–614) gp41(605–615 LAI) TAVPWNASW Vaccine human(B35) [Johnson (1994b)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- Epitope for vaccine induced CD8+ clone

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gp160(606–614) gp41(606–614 LAI) TAVPWNASW Vaccine human(B35) [Johnson (1994a)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees

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gp160(606–614) gp41(606–614 LAI) TAVPWNASW Vaccine human(B35) [Hammond (1995)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- Peptide only processed by a TAP-1/2-dependent pathway

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gp160(606–614) gp41(606–614) TAVPWNASW HIV-1 infection human(B35) [Ferris (1999)]

- This epitope is processed by a TAP1/2 dependent mechanism

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gp160(606–614) gp41( ) TAVPWNASW HIV-1 exposed seronegative human(B35) [Rowland-Jones (1998b)]

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes
- This epitope is conserved among A, B and D clade viruses

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gp160(606–614)	gp41(606–614)	TAVPWNASW	HIV-1 exposed seronegative, HIV-1 infection	human(B35)	[Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

gp160(634–648)	gp41(641–655 SF2)	EIDNYTNTIYTLLEE	HIV-1 infection	human( )	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- One of these 11 had CTL response to this peptide
- The responding subject was HLA-A1, A2, B51, and B57

gp160(678–686)	Env(679–687 clade B)	WLWYIKIFI	Vaccine	human(A2.1)	[Kundu (1998a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses

gp160(680–689)	gp41(679–687 SF2)	WYIKIFIFMI	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402
- This peptide induced CTL in 1/4 HIV-1+ people tested
- WYIKIFIFMI bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained

gp160(685–693)	Env(686–694 clade B)	FIMIVGGLV	Vaccine	human(A2.1)	[Kundu (1998a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses

gp160(700–708)	gp41(705–714)	AVLSVVNRV	HIV-1 infection	human(A2)	[Ferris (1999)]
• This epitope is processed by a TAP1/2 dependent mechanism					
gp160(701–720)	gp41(701–720 BH10)	VLSIVNRVRQGYSPLS-FQTH	HIV-1 infection	human(A32)	[Safrit (1994a)]
• Recognized by CTL derived from acute seroconverter					
gp160(704–712)	gp160(704–712 LAI)	IVNRNRQGY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001b)]
• C. Brander notes this is an A*3002 epitope					
gp160(704–712)	gp41( )	IVNRVRQGY	HIV-1 infection	human(A*3002)	[Goulder (2001a)]
• Epitope name: IY9 (gp41). HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant • In subject 199 four additional A*3002 epitopes were identified • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)					
gp160(747–755)	gp41(747–755)	RLVNGSLAL	HIV-1 infection	human(A2)	[Parker (1992)]
• Studied in the context of HLA-A2 peptide binding					
gp160(747–755)	gp41(741–749 CM243 CRF01)	RLVSGFLAL	HIV-1 infection	human(A2)	[Sriwanthana (2001)]
• Epitope name: E747-755. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2					
gp160(747–755)	gp41(741–749 CM243 CRF01)	RLVSGFLAL	HIV-1 infection	human(A2)	[Bond (2001)]
• HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested					

- 2/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids, RLVNGSLAL
- This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, C, and G

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gp160(754–768) gp41( ) ALIWEDLRSLCLFSY HIV-1 infection human(B55) [Jin (1998b)]

- Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction
- Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK

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gp160(767–775) gp41(766–774 SF2) SYRRLRDLL HIV-1 infection human(A*2402) [Ikeda-Moore (1997)]

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402
- This peptide induced CTL in 1/4 HIV-1+ people tested
- SYRRLRDLL bound to A*2402 moderately, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained

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gp160(767–780) gp41(606–614 LAI) SYHRLRDLLLIVTR HIV-1 infection human(A31) [Hammond (1995)]

- Peptide only processed by a TAP-1/2-dependent pathway
- CTL from an acute seroconverter

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gp160(769–777) gp41(769–777 BH10) HRLRDLLLI HIV-1 infection human( ) [Safrit (1994a)]

- Recognized by CTL derived from acute seroconverter

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gp160(770–778) Env(679–777) RLRDLLLIV HIV-1 infection human(A*0201) [Kmieciak (1998a)]

- Epitope name: 5.3. CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues
- The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*
- Peptides 5.3 and D2 bound to HLA A*0201 with low affinity and were variable, particularly D2;

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gp160(770–780) gp41(775–785) RLRDLLLIVTR HIV-1 infection human( ) [Betts (2000)]

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant
- Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes
- 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope that has been previously noted to be HLA A3.1, as well as seven others

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gp160(770–780) gp41(768–778 NL43) RLRDLLLIVTR HIV-1 infection human(A*0301) [Takahashi (1991)]

- CD8+ T-cell clone

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gp160(770–780)	gp41(775–785 LAI)	RLRDLLLIVTR	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*0301 epitope					
gp160(770–780)	gp41(770–780 BH10)	RLRDLLLIVTR	HIV-1 infection	human(A*3101)	[Safrit (1994a), Safrit (1994b)]
• Recognized by CTL derived from acute seroconverter • C. Brander notes that this is an A*3101 epitope in the 1999 database					
gp160(770–780)	gp160(770–780 LAI)	RLRDLLLIVTR		human(A*3101)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*3002 epitope					
gp160(770–780)	gp41(768–778 NL43)	RLRDLLLIVTR	HIV-1 infection	human(A3)	[Cao (1997)]
• The consensus peptide of clade B is RLRDLLLIVTR • The consensus peptide of clades A, C and E is RLRDFILIVTR and it is less reactive • The consensus peptide of clade D is SLRDLLLIVTR and it is less reactive					
gp160(770–780)	gp41(775–785)	RLRDLLLIVTR	HIV-1 exposed seronegative, HIV-1 infection	human(A3)	[Kaul (2001a)]
• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers					
gp160(770–780)	gp41(770–780)	RLRDLLLIVTR	HIV-1 infection	human(A3)	[Day (2001)]
• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant					
gp160(770–780)	gp41(770–780)	RLRDLLLIVTR	HIV-1 infection	human(A31)	[Ferris (1999), Hammond (1995)]
• This epitope is processed by a TAP1/2 dependent mechanism					
gp160(777–785)	gp41(782–790 LAI)	IVTRIVELL		human(A*6802)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*6802 epitope					
gp160(781–802)	gp120(788–809)	IVELLGRRGWEALKY-WWNLLQY	*in vitro* stimulation	human( )	[Lieberman (1995)]
• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide					

gp160(781–802)	gp41(788–809 HXB2)	IVELLGRRGWEALKY-WWNLLQY	HIV-1 infection	human(B27)	[Lieberman (1992)]
• CTL epitope defined by T-cell line and peptide mapping					
gp160(786–794)	gp41(791–799 LAI)	GRRGWEALK	HIV-1 infection	human(B27)	[McMichael & Walker(1994)]
• Review of HIV CTL epitopes • Also: J. Liebermann 1992 and pers. comm. J. Liebermann					
gp160(786–795)	gp41(791–800 LAI)	GRRGWEALKY	HIV-1 infection	human(B*2705)	[Brander & Goulder(2001)]
• C. Brander notes this is a B*2705 epitope					
gp160(786–795)	gp41(791–800 LAI)	GRRGWEALKY	HIV-1 infection	human(B27)	[Lieberman(1998)]
• Optimal peptide mapped by titration J. Lieberman, Pers. Comm.					
gp160(786–795)	gp41(786–795)	GRRGWEALKY	HIV-1 infection	human(B27)	[Day (2001)]
gp160(794–802)	gp160(794–802 LAI)	KYCWNLLQY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001b)]
• C. Brander notes this is an A*3002 epitope					
gp160(794–802)	gp41( )	KYCWNLLQY	HIV-1 infection	human(A*3002)	[Goulder (2001a)]
• Epitope name: KY9 (gp41). HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant • In subject 199 four additional A*3002 epitopes were identified • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)					
gp160(794–814)	gp41( )	KYCWNLLQYWSQELK-NSAVSL	HIV-1 infection	human( )	[Altfeld (2000)]
• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by a molecule other than B60 in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined					

gp160(795–816)	gp41(802–823 HXB2)	YWWNLLQYWSQELKN-SAVNLLN	HIV-1 infection	human( )	[Lieberman (1992)]

- CTL epitope defined by T-cell line and peptide mapping

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gp160(799–807)	Env(800–808 clade B)	LLQYWSQEL	Vaccine	human(A2.1)	[Kundu (1998a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses

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gp160(805–814)	gp41(810–819 LAI)	QELKNSAVSL		human(B*4001)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*4001,B60 epitope

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gp160(805–814)	gp41( )	QELKNSAVSL	HIV-1 infection	human(B60(B*4001)	[Altfeld (2000)]

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes
- B60 is present in 10-20% of the Caucasoid and very common in Asian populations

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gp160(805–814)	gp41(805–814)	QELKNSAVSL	HIV-1 infection	human(B60/B61)	[Day (2001)]

- No immunodominant responses were detected to five B61-restricted epitopes tested
- All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response

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gp160(813–822)	gp41(814–823 LAI)	SLLNATDIAV	Vaccine	human(A*0201)	[Dupuis (1995)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823
- Noted to be A*0201 in Brander *et al*., 1999 database

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gp160(813–822)	gp41(818–827 LAI)	SLLNATDIAV	Vaccine	human(A*0201)	[Brander & Goulder(2001)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- C. Brander notes this is an A*0201 epitope

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gp160(813–822)	gp41(814–823)	SLLNATDIAV	HIV-1 infection	human(A2)	[Kundu (1998b)]

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients

- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated
- SLLNATDIAV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, and 3 of these had a detectable CTL response – the other two had either the sequence SLFNAIDIAV or SLLNTTDIVV and no detectable CTL response
- CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine

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gp160(813–822) gp41(818–827) SLLNATDIAV HIV-1 infection human(A2) [Betts (2000)]

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant
- Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes
- 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes, including this epitope

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gp160(813–822) gp41( ) SLLNATAIAV HIV-1 infection human(A2) [Goulder (2001b)]

- Epitope name: SV10. Dominant CTL epitope in acute infection of patient AC13– response to this epitope corresponded to reduction of initial viremia
- Several other subdominant CTL epitopes were identified in the acute phase, but a response to SL9, SLYNTVATL, was not evident until 18 months post-presentation

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gp160(813–822) gp41(77–85 SF2) SLLNATDIAV HIV-1 infection human(A2) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 1/4 group 3

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gp160(813–822) gp41(814–823 CM243 CRF01) SLLNATAIAV HIV-1 infection human(A2) [Sriwanthana (2001)]

- Epitope name: E813-82. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2

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gp160(813–822) gp41(814–823 CM243 CRF01) SLLNATAIAV HIV-1 infection human(A2) [Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested

- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by one amino acid, SLLNATDIAV
- This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, D, and F

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gp160(813–822) gp41(813–822) SLLNATDIAV HIV-1 infection human(A2) [Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person

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gp160(813–822) Env(814–823 clade B) SLLNATDIAV Vaccine human(A2.1) [Kundu (1998a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses
- CTL to overlapping peptides in this region gave a positive response in the greatest number of patients
- ALTERNATIVE EPITOPES: LLNATDIAV and LLNATDIAVA – CTL were induced by vaccine in those that had the sequence SLLNATAIAVA in their own infection, but not in those with: NLLNTIAIAVA or NLFNTTAIAVA or SLLNATAITVA

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gp160(813–822) gp41( ) SLLNATDIAV HIV-1 infection human(A68) [Altfeld (2001d)]

- Epitope name: gp41 SV10. HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acutely infected individuals recognized at least 1 (median of 1 and maximum of 2)
- This epitope binds to three HLA-A2 supertype alleles: A*6802 (highest affinity), A*0202 and A*0203 (but not A*0201 and not A*0206)
- This epitope did not elicit an ELISPOT response in 22 chronic HIV HLA-A2 infections, but elicited a strong response in 1/12 acute HLA-A2 infections – this individual, AC13, was HLA A*0201/68 B44/14 and also had a strong response to HLA-A2 vpr epitope AIIRILQQL

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gp160(814–822) Env(815–823) LLNATAIAV HIV-1 infection human(A*0201) [Kmieciak (1998a)]

- Epitope name: D2. CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues;
- The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*;
- Peptides 5.3 and D2 bound to HLA A*0201 with low affinity and were variable, particularly D2;
- Substitutions in peptide D2: `---TI----` did not abrogate the response, but diminished it;
- In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher;

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gp160(814–822) gp41(815–823 LAI) LLNATDIAV Vaccine human(A2) [Dupuis (1995)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823

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gp160(814–822) Env(815–823) LLNATAIAV HIV-1 infection human(A2) [Kmieciak (1998b)]

- Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product

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gp160(822–832) gp41( ) VAEGTDRVIEI HIV-1 infection human( ) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of individuals that had a CTL response to this epitope (HLA presenting molecule uncertain) broken down by group: 0 group 1, 1 group 2, and 0 group 3

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 exposed seronegative human( ) [Pinto (1995)]

- Epitope name: HP53. CTL and T helper cell reactivity in healthcare workers exposed to HIV

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR HIV-1 infection human(A2) [Clerici (1991)]

- Epitope name: HP53. Helper and cytotoxic T-cells can be stimulated by this peptide (Th4)

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR Vaccine murine(H-$2^{d,p,u,q}$) [Shirai (1992)]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Epitope name: HP53. In a murine system multiple class I molecules can present to CTL

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gp160(827–841) gp41(834–848 IIIB) DRVIEVVQGAYRAIR Vaccine murine(H-$2^{d,p,u,q}$) [Shirai (1996)]

Vaccine: *Vector/type:* vaccinia *HIV component:* gp160

- Epitope name: HP53. Multiple murine MHC can cross-present this epitope, and P18, RIQRGPGRAFVTIGK, to specific CTL

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gp160(828–836)	gp41(829–837 LAI)	RVIEVLQRA	Vaccine	human(A2)	[Dupuis (1995)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- CTL from HLA-A2 positive subject react with this peptide

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gp160(828–836)	gp41(829–837 CM243 CRF01)	KVIEVAQGA	HIV-1 infection	human(A2)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by three amino acids, RVIEVLQRA
- This epitope was only conserved in CRF01 (subtype E), and identities were rare

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gp160(828–836)	Env(829–837 clade B)	RVIEVLQRA	Vaccine	human(A2.1)	[Kundu (1998a)]

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp160

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual
- CTL responses after reimmunization may include recall responses – individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses

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gp160(830–854)	gp41(831–853)	IEVVQGAYRAIIRHIPR-RIRQGLERI	HIV-1 infection	human( )	[Price (1995)]

- Study of cytokines released by HIV-1 specific activated CTL

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gp160(835–843)	Env(834–842 SF2)	RAYRAILHI	HIV-1 infection	human(B*5101)	[Tomiyama (1999)]

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed
- This peptide could stimulate CTL from one person, however this CTL clone did not recognize B*5101 positive target cells infected with HIV-1 recombinant vaccinia expressing Env, so it was not confirmed that this peptide was a properly processed epitope

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gp160(837–856)	gp120(844–863)	YRAIRHIPRRIRQGLER-ILL	*in vitro* stimulation	human( )	[Lieberman (1995)]

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide

gp160(837–856)	gp120(844–863 SF2)	YRAIRHIPRRIRQGLER-ILL	HIV-1 infection	human( )	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160
- One of these 11 had CTL response to this peptide
- The responding subject was HLA-A2, A26, B7, and B38

gp160(837–856)	gp120(844–863 LAI)	YRAIRHIPRRIRQGLER-ILL	HIV-1 infection	human(B35)	[Shankar (1996)]

gp160(837–856)	gp41(844–863 HXB2)	YRAIRHIPRRIRQGLER-ILL	HIV-1 infection	human(B8)	[Lieberman (1992)]

- CTL epitope defined by T-cell line and peptide mapping

gp160(842–856)	gp41( )	HIPRRIRQGLERALL	HIV-1 infection	human( )	[Altfeld (2001a)]

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses is underestimated if accessory proteins are not included in the study
- The only Env peptide recognized was gp41 HIPRRIRQGLERALL

gp160(843–851)	gp41(848–856 LAI)	IPRRIRQGL		human(B*0702)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*0702 epitope

gp160(843–851)	gp41(848–856 LAI)	IPRRIRQGL		human(B7)	[Brander & Walker(1995)]

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study

gp160(843–851)	( )	IPRRIRQGL	HIV-1 infection	human(B7)	[Soudeyns (1999)]

- Following primary infection, progressive diversification and accumulation of mutations of HIV-env nucleotide sequences was observed, focused in V2 in one individual and in V8 in another
- The patient with the V2 diversification showed only transient CTL against Env and Nef
- The patient with the V8 diversification had an immunodominant CTL response to V8 epitope IPRRIRQGL, and multiple escape variants emerged within a year: `--T------` and `--T-----F`, which abrogated the CT response *in vitro*, and also`----L---` and `-------D-` which gave diminished responses

gp160(843–851)	gp41(848–856 LAI)	IPRRIRQGL	HIV-1 infection	human(B7)	[Cao (1997)]

- The consensus peptide of clades A, B, D, and F is IPRRIRQGL
- The consensus peptide of clade C is IPRRIRQGF, and it is equally reactive

gp160(843–851)	gp41(848–856 clade B)	IPRRIRQGL	HIV-1 infection	human(B7)	[Wilson (1998b)]

- The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed
- Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope IPRRIRQGL is conserved between the LAI and clade A and C strains, but that MN has a non-conservative Arg to Thr substitution at position three that may be contributing to the specificity of the response in the HLA B7 individuals

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gp160(843–851)	gp41(843–851 HXB2)	IPRRIRQGL	HIV-1 infection	human(B7)	[Hay (1999)]

- CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201
- The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted
- Despite the initial narrow response to two epitopes, no other CTL responses developed
- No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak
- Variants were observed *in vivo*, the most common form of the viral epitope at presentation at 3 months was the only form that did not elicit a CTL response: `----T----`; the other forms detected were `--------F`, `-----L--F`, `V-------F` and they could elicit a CTL response although the response to `-----L--F` was reduced
- A second rapid progressor had a detectable CTL response exclusively to this epitope

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gp160(843–851)	gp41( )	IPRRIRQGF	HIV-1 infection	human(B7)	[Cao (2000)]

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent-specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype
- This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection, is cross-reactive with subtypes A and B, but not in subtype D

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gp160(843–851)	gp41( )	IPRRIRQGL	HIV-1 infection	human(B7)	[Islam (2001)]

- Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS
- This individual had a dominant response to IPRRIRQGL with strong *in vivo* activated responses and *in vitro* stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred within both epitopes

- At 3 months post-presentation, seven IPRRIRQGL CTL clones were obtained, five used the T-cell receptor Vβ 6S1 and Jβ 2.7 and had the CDR3 WAASS, two used Vβ16S1, ERSPPGD, Jβ 2.7 and one CTL clone isolated at 39 months was Vβ 14S1, CR3 PTAAG, and Jβ 2.1 – all of these clones persisted over the course of the infection, even to time of death, despite the loss of CTL functional responses over time

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gp160(843–851) gp41(843–851 SF2) IPRRIRQGL HIV-1 infection human(B7) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 2/4 group 1, 1/3 group 2, and 1/1 group 3

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gp160(843–851) gp41(848–856) IPRRIRQGL HIV-1 exposed seronegative, HIV-1 infection human(B7) [Kaul (2001a)]

- IPRRIRQGL cross-reacts with clades A, B and D
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-B7 women, 2/5 HEPS and 5/6 HIV-1-infected women recognized this epitope
- The dominant response to this HLA allele was to this epitope in 2 of the 5/6 HIV-1-infected women that responded to the epitope, but in neither of the 2/5 HEPS cases
- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV

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gp160(843–851) gp41(843–851) IPRRIRQGL HIV-1 infection human(B7) [Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes

- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope

gp160(843–851)	gp41( )	IPRRIRQGL	HIV-1 infection	human(B7)	[Altfeld (2000)]
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by a molecule other than B60 in an HLA-B60 individual				
gp160(845–856)	gp41(852–863 HXB2)	RRIRQGLERILL	HIV-1 infection	human(A30, B8)	[Lieberman (1992)]
	• CTL epitope defined by T-cell line and peptide mapping				
gp160(845–856)	gp41(852–863 LAI)	RRIRQGLERILL	HIV-1 infection	human(B7)	[Shankar (1996)]